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VOL. 49 APRIL, 1955 No. 4

AMERICAN HEART JOURNAL

AN INTERNATIONAL PUBLICATION FOR THE STUDY OF THE CIRCULATION

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UNIVERSITY OF MICHIGAN
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Vol. 49, No. 4, April, 1955, American Heart Journal is published monthly, by The C. V. Mosby Company, 3207 Washington Avenue, St. Louis 3, Missouri, entered as second class matter January 23, 1917 at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Additional entry authorized at Jefferson City, Missouri. Subscription Price: United States, and its Possessions, per year $12.00; Canada $13.00; Foreign $13.50. Printed in the U. S. A.

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American Heart Journal

VOL. 49 APRIL, 1955 No. 4

Original Communications

CLINICAL INVESTIGATION BY THE OSCILLOGRAM OF PERIPHERAL ARTERIES

M. G. KETTNER, M.D.,* C. FERRERO, M.D., AND P. W. DUCHOSAL, M.D.

GENEVA, SWITZERLAND

INTRODUCTION

THIS investigation was undertaken to study in some detail the pulse curve recorded from a pressure cuff around an extremity. The size and shape of the pulse curve, as well as its time relationship to electrical events of the cardiac cycle, were evaluated. An attempt was made to determine whether the size of the curve alone is significant, in arterial disease, or if its form and timing also show important changes. For this purpose a differential manometer was constructed to record accurately on film the same arterial oscillations observed when clinical oscillometers, such as the Pachon or von Recklinghausen instruments, are used. A random general sampling, both of normal subjects and of patients with various diseases of the heart and blood vessels, was taken and the results analyzed.

APPARATUS

The construction of the differential manometer is based on the principle of the torsion-tension relationship of a twisted metal band. A bronze band, 10 cm. in length, 1 mm. in width, and 0.5 mm. in thickness, with rectangular perforations of 0.5 by 1.0 mm. dimensions separated by narrow bands 0.2 mm. wide, is twisted at its middle about its long axis. This results in a separate spiral running from the middle to each end of the band, one turning clockwise, the other counterclockwise.

One end of this double spiraled band is fixed, the other is attached to the movable membrane of the metal capsule of the pneumatic system. A change in tension of the metal band, brought about by movement of the membrane, produces a change in its torsion, thus effecting a rotation of its spiral turns about its long axis.

Mirrors are mounted on the band at three locations between the middle and the fixed end, all facing forward in the same plane. For a given change in tension of the band, the size of the arc of rotation of each of these mirrors is directly proportional to its distance from the end (the

From the Centre de Cardiologie, Hôpital Cantonal de Genève.

Received for publication Sept. 24, 1954.

*Dr. Kettner's work was supported in part by a grant from the American-Swiss Foundation for Scientific Exchange, Inc., administered through the Institute of International Education.

mirror directly at the middle rotates through the greatest arc, and that near the end through the smallest). Mirrors mounted below the middle toward the lower end of the band would have equivalent but opposite arcs of rotation from their counterparts mounted on the upper one-half.

The metal band and capsule are mounted in a rectangular, air-tight, metal box with a Plexiglass window along its face, to transmit light (Fig. 1). Light from a fixed source reflected from the moving mirrors to a continuous film produces an accurate curve of the pulse wave being studied. The level of the light source is adjustable and can be focused on any of the three mirrors, thus allowing a selection of the sensitivity desired (greatest sensitivity is obtained with the mirror mounted near the middle, least with the mirror mounted near the end). The fixed tension of the metal band may be adjusted by means of a thumbscrew. This allows recordings to be made with the same fixed band tension. The metal box may also be moved up or down, or be rotated, permitting great freedom of movement for properly centering the reflected light on the film.

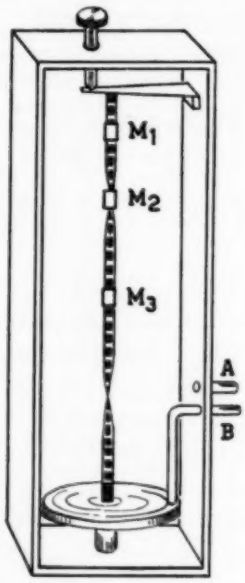


Fig. 1.

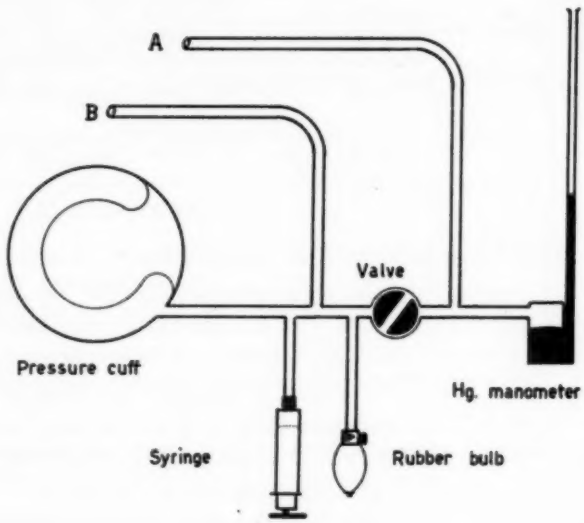


Fig. 2.

Fig. 1.—A drawing of the differential manometer based on the principle of the metal torsion band. M_1, M_2, M_3 are mirrors. *A* is the inflow to the membrane of the capsule. *B* is the inflow to large chamber.

Fig. 2.—A schematic diagram of the pneumatic circuit.

The pneumatic system itself consists of two circuits connected by a valve (Fig. 2). One circuit contains a mercury manometer connected with the air-tight metal box enclosing the spiraled band. The other consists of an ordinary blood pressure cuff, a hypodermic syringe for standardization, and the flat circular metal capsule with movable membrane. With the valve open between the two circuits, the cuff is inflated to the desired counterpressure, which at this point is the same everywhere in the pneumatic system. The valve is then closed, and pressure changes in the cuff are exclusively transmitted to the membrane, band, and mirror, as described previously. During this time the environment pressure, inside the metal box, remains constant at the level existing when the valve was closed.

An accurate standard is obtained by modifying the volume of the recording side of the pneumatic system by an exactly measured amount. A hypodermic syringe incorporated into the system is used for this purpose. This known change in volume elevates the base line of the record. This increment can be measured accurately.

A small rubber cuff was constructed for recording pulsations from the fingers and toes. A smoothly coated pneumatic cuff placed around the neck allowed good recordings of the carotid pulsations. The electrocardiogram, the counterpressure of a second cuff (when the two-cuff

system is used, as in blood pressure recordings), and the respiratory cycle may also be recorded simultaneously. These additional recordings require suitable mirror arrangements and separate light sources.

The response and fidelity of the instrument are shown by a simultaneous recording with a Statham pressure transducer of artificially induced pressure changes in an inflated cuff (Fig. 3).

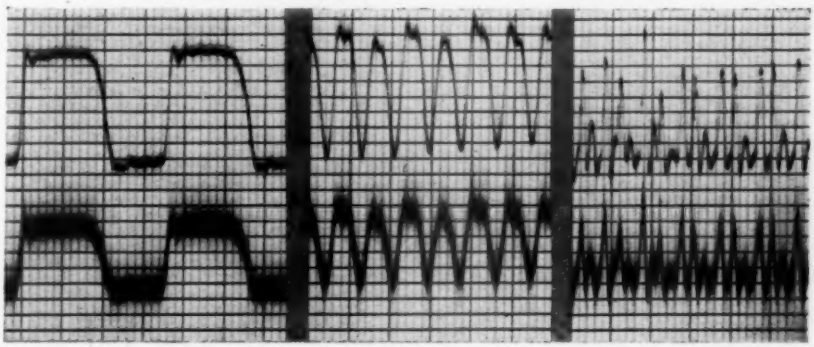


Fig. 3.—A simultaneous recording of artificial impulses with the differential manometer (upper tracing) and a Statham pressure transducer (lower tracing), showing high fidelity over a wide frequency range.

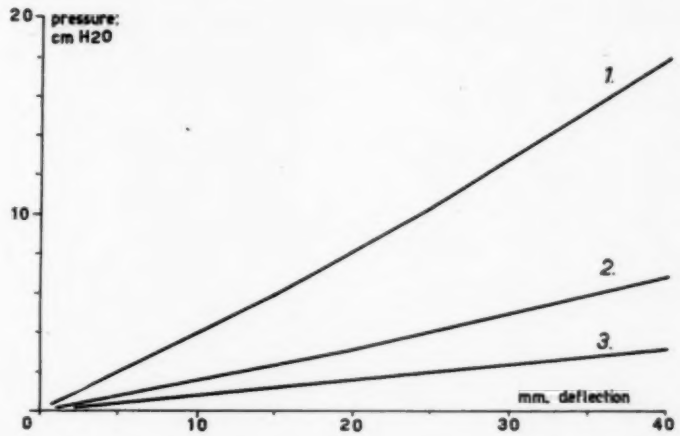


Fig. 4.—Calibration of the sensitivities of the three mirrors of the differential manometer, showing very nearly linear responses for deflections up to 40 mm. (full scale). The ratios for the three sensitivities as calculated from this curve are 6.22, 2.69, and 1.

Results of calibration with a water manometer are shown in Fig. 4. Since the response is very nearly linear for the smallest to the largest deflections at all three sensitivities, a relative constant relationship exists among the three. This relationship was calculated by taking an average of the values found at eight separate points on the scale and may be expressed in whole numbers as follows: 6.22, 2.69, and 1.0, representing the relative sensitivities of the lowest, the middle, and the highest placed mirrors, respectively.

METHOD

The investigations were begun by recording pulsations at successively descending levels of counterpressure; but, due to the many complex patterns

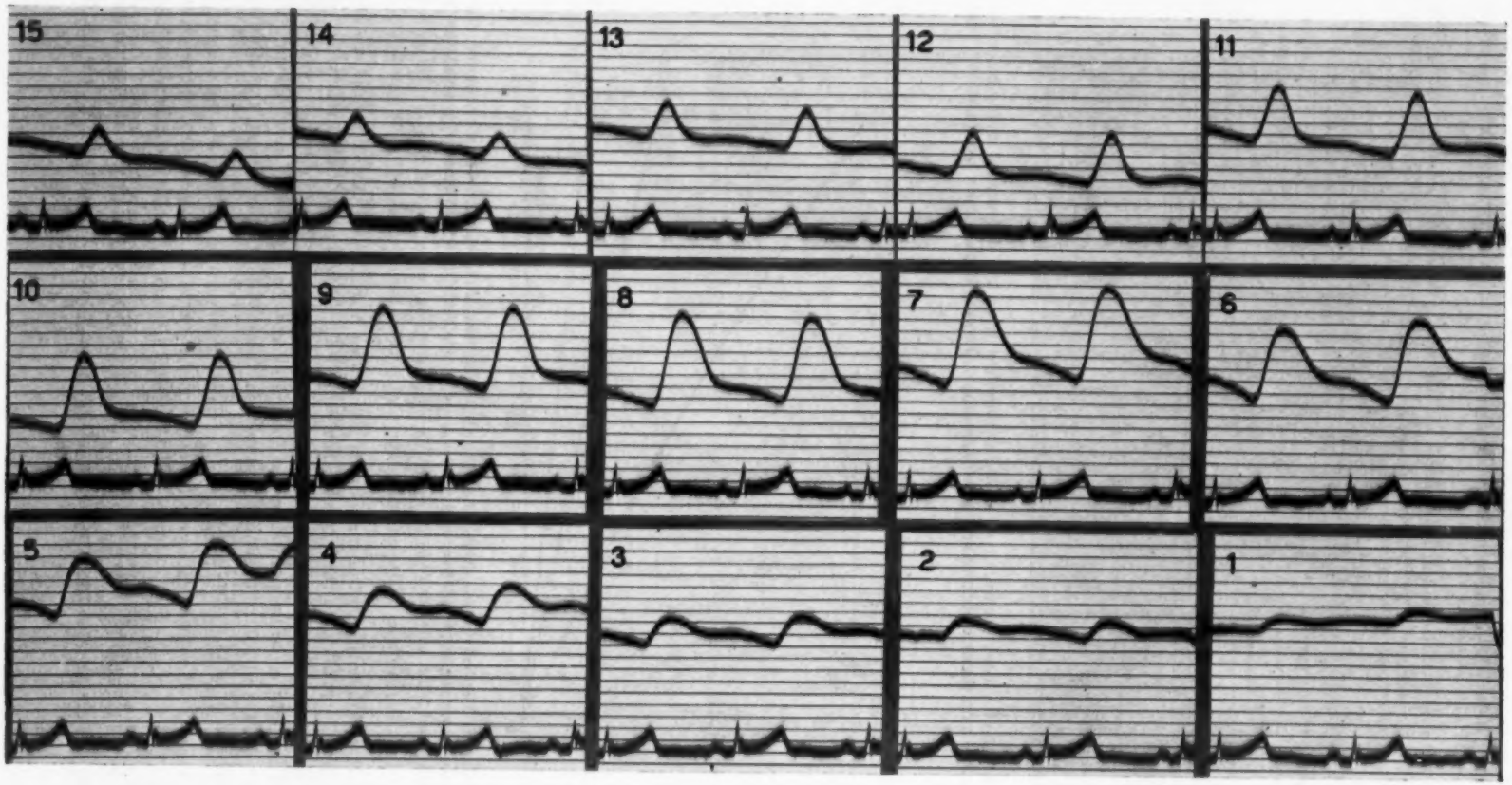


Fig. 5.—Oscillographic tracing of the ankle of a normal 20-year-old girl at successively descending levels of counterpressure from 150 to 10 mm. Hg, showing changes in shape and size until diastole is reached, after which changes in size alone are seen. Simultaneous ECG, Lead I. Blood pressure, left arm 105/65 mm. Hg.

(Fig. 5) and the distortions caused by compression of the artery when the counterpressure exceeds the diastolic pressure, the remainder of the pulse wave forms were recorded with a single infra-diastolic level of counterpressure, generally 50 mm. Hg. Tracings made at supra-diastolic levels were used only to approximate the cases of complete arterial obstruction. It was found that at all levels below diastole the pattern of the wave was the same and that only the volume changed, in accordance with the principles of Boyle's Law.

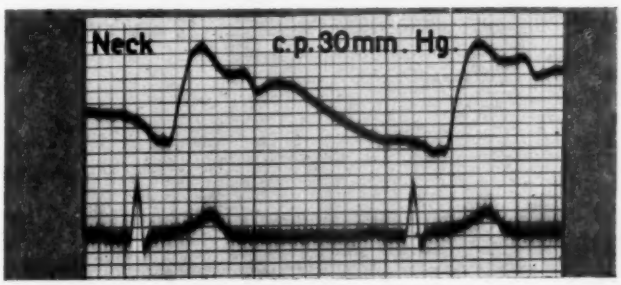


Fig. 6.—A recording from the carotid arteries obtained from a cuff around the neck.

Recordings were made from the forearm, index finger, and ankles in most of our subjects, and occasionally from the toes, upper arm, thigh, calf, or neck. A typical example of a normal record from the neck is illustrated in Fig. 6. Most of the subjects were given nitroglycerin as a test for vasodilation, recordings being made both before and after the drug. A study of similar nature has been reported by Foley and others.[2] This was done by using two cuffs, the upper, or compression cuff, having a pressure gradually descending from above systole to zero; and the lower, or recording cuff, having a constant counterpressure of 50 mm. Hg. The curves thus obtained were interpreted using criteria summarized by Ejrup in his recent monograph.[3] All subjects were examined in the same room in which the temperature varied between 18° and 21° C. It was not possible to control such factors as humidity, movement of air, etc., and no attempt was made to control the metabolic level of the subjects. On the ankle, the cuff was placed just above the malleoli, on the upper arm just above the antecubital fossa, and on the forearm just below the antecubital fossa. The rubber finger cuff was placed as near the base of the finger as possible.

An accurate standardization was made with each individual tracing on the last fifty-five subjects examined, using the hypodermic syringe to modify the volume by an exact measured amount. The lowest sensitivity was used in standardizing, and immediately switched to high sensitivity for the pulse recording. In this way, the error from spontaneous shifts of the base line was minimized. From the standard, the pulse volume before and after nitroglycerin was calculated and expressed in cubic centimeters.

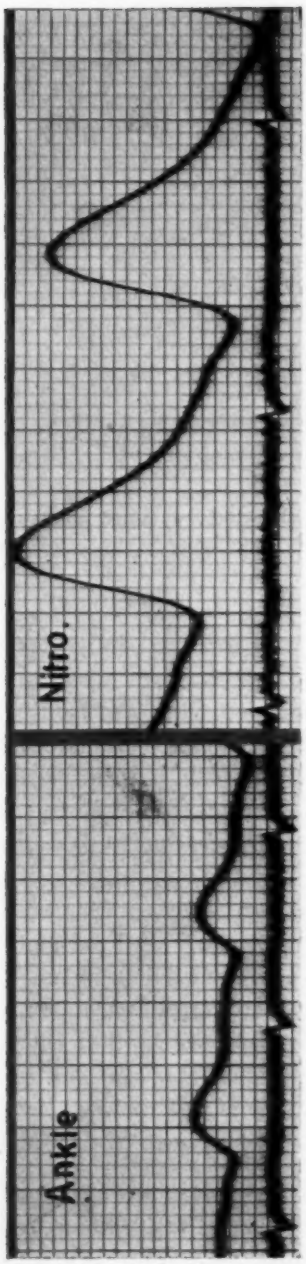
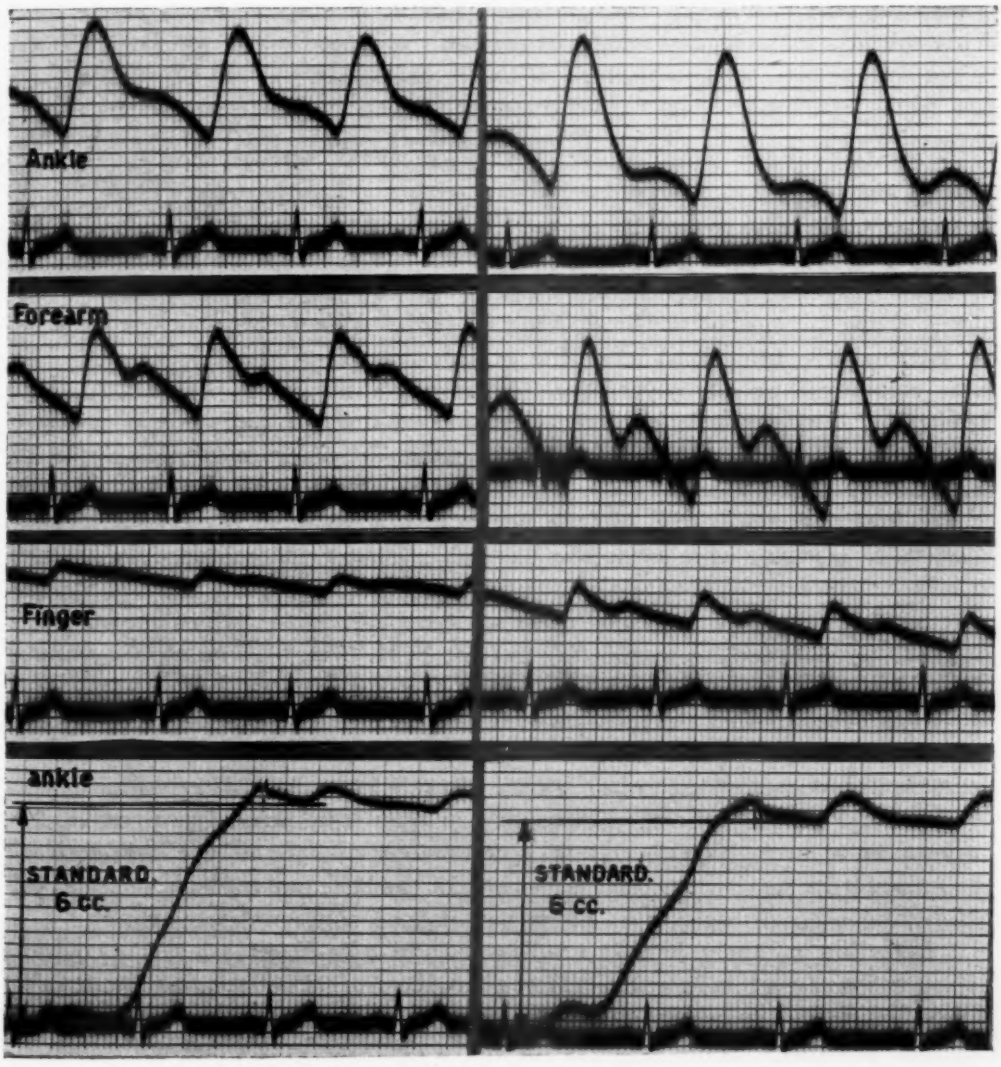


Fig. 7.—Ankle oscillogram of patient B.H., a normal 29-year-old woman. The pulse volume before nitroglycerin is 0.11 c.c. the smallest seen in our series of normals. The volume following the drug is 0.59 c.c., representing the greatest per cent increase seen in the normal group.

SUBJECTS

Tracings of ankle pulsations on one or both sides were made on a total of 127 subjects. In over two-thirds, additional tracings were made of finger pulsations. In over one-half of the total, tracings were also taken from the forearm. Pulsations were recorded from other locations of special interest in certain cases (upper arm, thigh, toes, neck). Fifty-eight of these subjects were considered normal for the purposes of this study (no symptoms or signs of cardiovascular disease, and no disease thought likely to affect the shape or size of the pulsations), with ages varying from 16 to 81 years. Forty-four of the subjects had signs and/or symptoms of arterial disease. The remaining twenty-five had no signs



A. *B.*

Fig. 8.—Oscillograms of the left forearm, index finger, and ankle, before (*A*) and after nitroglycerin (*B*), in patient J.G., a normal 31-year-old male. The standardization is with the ankle tracings (see text).

or symptoms of arterial disease itself but had either diseases known to be frequently associated with arterial disease (diabetes, hypertension) or other diseases which would be expected to alter the pulse pattern from the normal (valvular lesions, arrhythmias, pulsus alternans). A total of 102 subjects received nitroglycerin (50 normal and 52 with disease), with records made before and after medication. The initial studies were done with a rather large oral dose of nitroglycerin (0.00065 Gm.). Because of frequent discomfort (one patient, B. H., Fig. 7, had a transitory hypotensive episode) the dose was gradually reduced and finally standardized at 0.00025 Gm. With this dose there were no more undesirable side effects.

All the tracings described were taken with a counterpressure of 50 mm. Hg unless otherwise specified. The postnitroglycerin tracings were all begun four to five minutes following the administration of the drug.

RESULTS

Normals.—(Fifty-eight subjects, fifty received nitroglycerin.) All the normals exhibited a similar pulse pattern with good amplitude. The peak of the wave was always symmetrical, rather slender and somewhat pointed. The ascending and descending limbs tended to form a rather acute angle near the peak (also dependent upon the paper speed and the height of the wave). Most curves showed a notch on the descending limb. When this was not present, the entire wave tended to have the symmetrical form described here. The pulse volume before nitroglycerin varied from a minimum of 0.11 c.c. (patient B. H., Fig. 7) to a maximum of 1.04 c.c. but was most often near the average of these two extremes. A tracing from a typical normal subject is shown in Fig. 8.

Following nitroglycerin, all the normals showed an increase in amplitude of pulsation, ranging from a barely measurable 0.04 c.c. increase in pulse volume to 0.71 c.c. increase. By far the greatest number, however, showed a volume increase ranging near the middle of the scale between these two extremes. The greatest per cent increase was seen in patient B. H. (Fig. 6), whose pulse volume changed from 0.11 c.c. before nitroglycerin to 0.50 c.c. afterward.

Most cases showed a depression of the notch of the descending limb toward, and occasionally below, the base line. Frequently, there was a small transitory decrease in blood pressure and an increase in pulse rate following administration of the drug. This occurred particularly in our earlier cases receiving rather large doses of nitroglycerin. Often, spontaneous changes in size and shape of the pulse forms, as well as larger pulsations of the base line itself, were seen both before and after nitroglycerin. This has also been described by Burch.[4]

In certain instances, both supra-diastolic and infra-diastolic levels of counterpressure were used before and after nitroglycerin. The greatest increase in pulse volume was occasionally seen following nitroglycerin using the infra-diastolic pressure. Some subjects showed a decrease in volume with counterpressure above diastole and an increase in volume below diastole. The largest pulse volume seen following nitroglycerin was 1.75 c.c., observed in the same subject who showed the largest volume before the drug.

Recordings of the finger pulsations, made in a large percentage of this group, ranged from barely visible pulsations to those of considerable size, and had a great variety of forms. We were unable to establish any consistent pattern in these tracings from the finger.

Arterial Disease.—(Forty-four patients, thirty-three with nitroglycerin.) All of this group had definite signs and/or symptoms of arterial disease.

1. *Arteriosclerosis obliterans*: Thirty-five patients had arteriosclerotic disease of the lower extremities. Twenty-seven of them had ankle tracings which were unquestionably quite different from those seen in the normal series. The pulsations were in general, small (some practically nonexistent), flat, or bizarrely rounded at the peak. The response to nitroglycerin was quite poor. Several patients even showed a decrease in pulse volume after the drug. A typical example of an ankle tracing from this group is shown in Fig. 9. Six of these twenty-seven patients had a blood pressure in one or both legs which was lower than that of the arms. In these cases the pulsations were greatest when an infra-diastolic counterpressure was used. One of the six, M.J., had left common iliac obstruction demonstrated by aortography, and severe claudication of the left leg. He had an adequate pulse volume of 0.24 c.c. which increased to 0.34 c.c. following administration of nitroglycerin. The shape, however, was quite bizarre and different from the normal (Fig. 10). Some of the twenty-seven showed unilateral abnormalities, the asymptomatic or less symptomatic leg giving a normal tracing.

Five of the group had tracings that could not be distinguished in any way from those of the normals. Tracings from the remaining four were equivocal.

2. *Unequal radial pulses*: Three patients were observed clinically to have unequal arm pulsations. All three showed a marked discrepancy in pulse volume, form, and blood pressure between the two arms. Two of them also had intermittent claudication and showed equivocal ankle tracings.

3. *Buerger's disease*: A 29-year-old male, with probable Buerger's disease, had had intermittent claudication of the left leg for nine years. Two weeks prior to examination he had suffered a myocardial infarction. The tracings showed a marked discrepancy in size between the two ankles.

4. *Other*: Three cases of Raynaud's phenomenon, one case of periarteritis nodosa and one patient with chronic ulceration of the toe were also examined. None of these exhibited definite findings.

Other Diseases.—(Twenty-five patients, nineteen with nitroglycerin.) This group included those subjects having diseases frequently associated with arterial disease, or other disease which would be expected to alter the size or shape of the pulse wave.

1. *Inactive rheumatic valvulitis with aortic insufficiency*: Six patients with varying degrees of aortic regurgitation were studied. One tracing was definitely abnormal by virtue of an abrupt onset of the upstroke. This is consistent with the rapid ejection phase described in aortic insufficiency. Two patients had

Fig. 9.

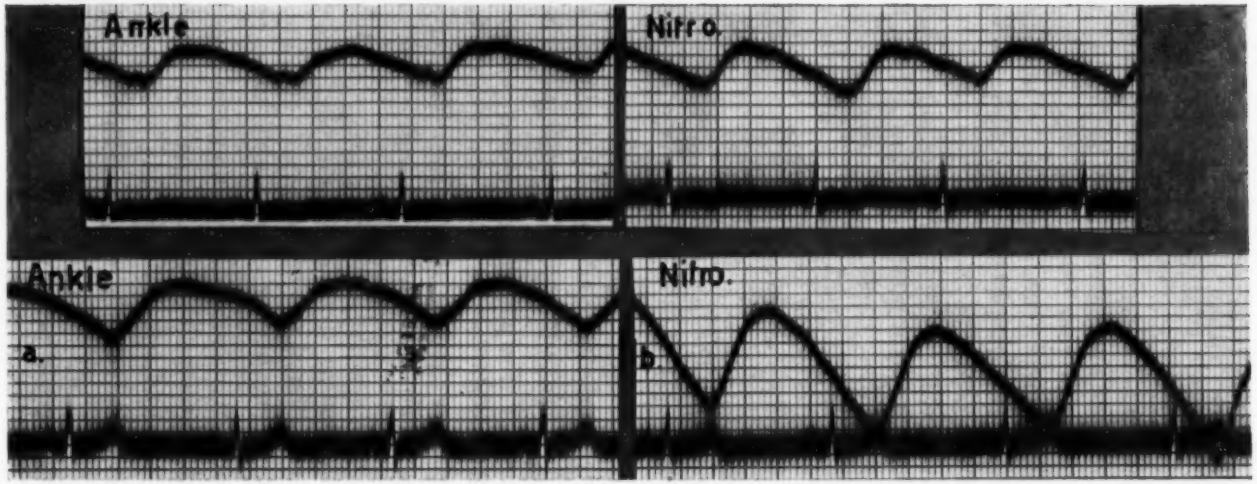


Fig. 10.

Fig. 9.—Left ankle oscillograms of patient E.A., a 63-year-old male with arteriosclerosis obliterans and intermittent claudication of both legs, showing small volume, abnormal shape, and poor response to nitroglycerin.

Fig. 10.—Left ankle oscillogram of M.J., a 50-year-old male with complete obstruction of the left common iliac artery and a left sympathectomy. Systolic pressure in this leg was 90 mm. Hg before nitroglycerin (*a*) and 105 mm. after (*b*), while in the left arm it was 125 mm. before and 120 mm. after.

equivocal irregularities. One, with associated stenosis of the valve, had a small, rounded wave of normal shape.

2. *Aortic aneurysm* (syphilitic): Two patients were examined. One had a normal tracing; the other patient had an abrupt rapid upstroke. He also had a wide pulse pressure with a blood pressure of 210/60 mm. Hg.

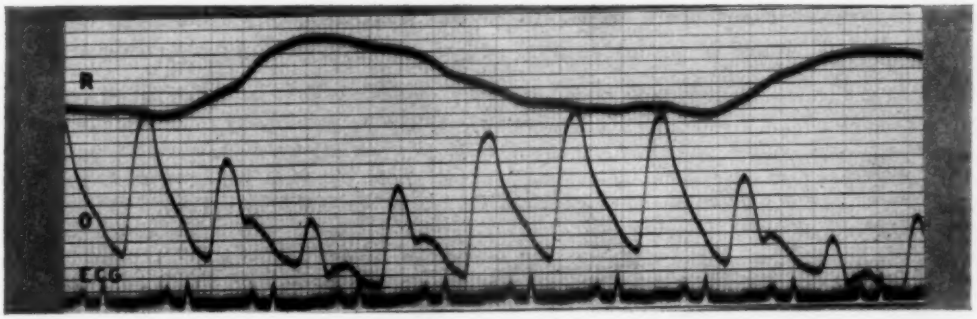


Fig. 11.—Simultaneous recording of the respiration, electrocardiogram, and upper arm oscillogram (counterpressure 140 mm. Hg) of R.D., a 13-year-old male, with tuberculous constrictive pericarditis, exhibiting marked pulsus paradoxicus.

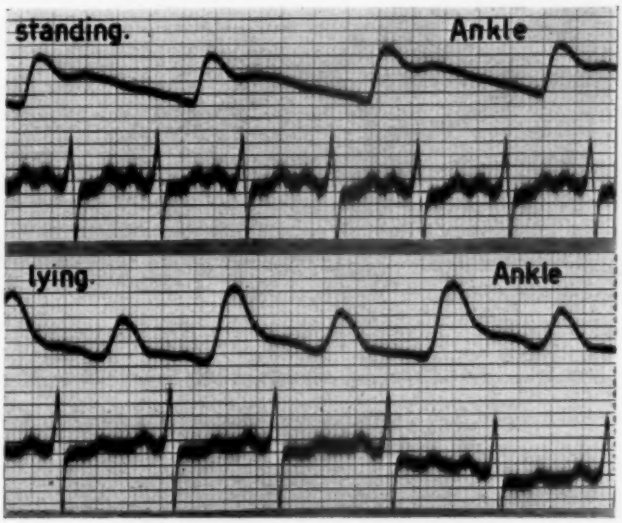


Fig. 12.—An oscillogram from the left ankle (counterpressure 140 mm. Hg) of C.V., a 28-year-old male with hypertensive cardiovascular disease with congestive failure, showing a pulsus alternans which was so marked when standing that alternate beats are almost absent.

3. *Hemodynamic disturbances*: One case of constrictive pericarditis with marked pulsus paradoxicus, Fig. 11, and one case of marked pulsus alternans, Fig. 12, were examined, both showing abnormalities of interest.

4. *Arrhythmias*: One patient with auricular fibrillation and one with complete heart block showed abnormalities attributable to the arrhythmias (Figs. 13 and 14).

5. *Coarctation*: Two cases were studied. Both showed only equivocal changes. Both had adequate pulsations of the lower extremities. While the systolic pressure was greater in the arms, both had normal pressures in the legs.

6. *Miscellaneous*: Eleven other subjects examined showed no definite abnormalities. They were patients with hypertension, diabetes, coronary artery disease, fever of undetermined origin and patent ductus arteriosus.

Fig. 13.

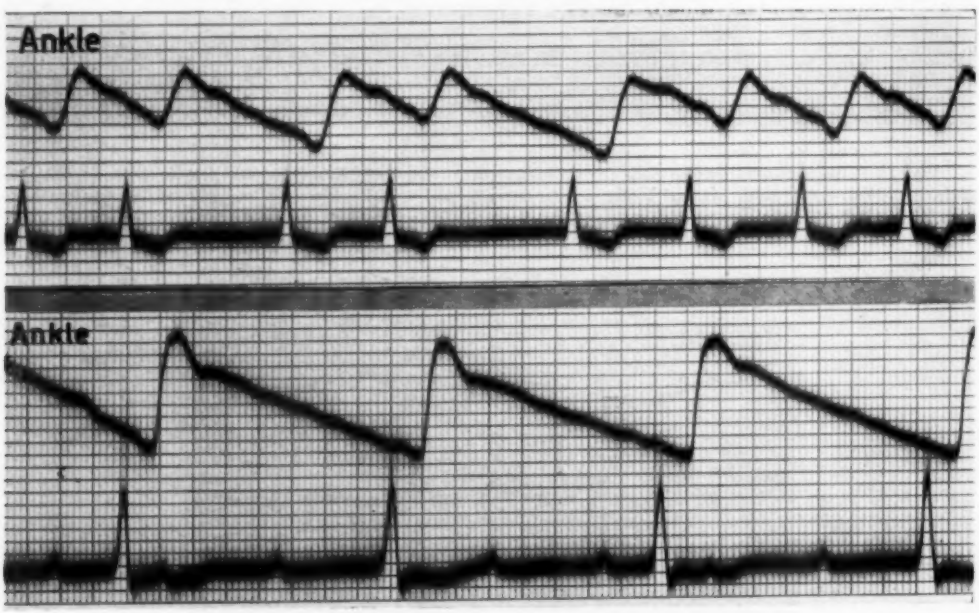


Fig. 14.

Fig. 13.—Ankle oscillogram of J.L., a 63-year-old patient with hypertension and auricular fibrillation.

Fig. 14.—Ankle oscillogram of H.W., a 59-year-old male, showing complete A-V block.

DISCUSSION AND CONCLUSIONS

All the recordings were interpreted according to principles of oscillometry, i.e., a change in volume of a limb during the passage of the pulse wave produces a corresponding change in volume of the surrounding inflated pressure cuff. When a pressure change occurs inside the cuff, a pulse wave may be recorded. This results in a segmental plethysmogram recorded against a counterpressure of 50 mm. Hg, or more. The counterpressure eliminates venous pulse waves or other volume changes in the limb which exert a pressure below this figure.

Therefore, a great deal of the knowledge of plethysmography may be applied directly to the study of oscillometry (the measurement of oscillations) and oscillography (the recording of the oscillations).

The physical laws governing the volume-pressure changes involved in oscillometry and its allied studies are embodied in Boyle's law. The law may be expressed in the following according to Mariotte (from Müller[1]).

$$\frac{B + P + p}{B + p} = \frac{V}{V - v}$$

B is the barometric pressure. *P* is the counterpressure of the cuff. The *p* is the pressure change produced by the pulsation. B, P and *p* are all expressed in centimeters of mercury. *V* is the volume of the inflated cuff. The change in volume produced by the pulsation is *v*. Both are expressed in cubic centimeters. One can obtain the pulsatile change in volume of the limb segment being examined as follows: (1) Measure the height of the deflection produced by a standard of known volume. (2) Convert this figure to pressure by use of the calibration data of Fig. 4. (3) Substitute values in the above formula. (4) Solve for *V*. (5) Having determined *V*, repeat the process, using the measurement (maximal deflection of the pulse wave itself), and solving for v.

The determination may be made from a simple proportion. The volume of the known standard produces a standard deflection which can be measured. The volume of the pulse wave (the unknown) creates a pulse deflection which can be measured. The proportion is expressed mathematically as

$$\frac{\text{volume of standard}}{\text{deflection of standard}} = \frac{\text{volume of pulse}}{\text{deflection of pulse}} \times \text{constant.}$$

The constant 6.22 is used because the sensitivity used for recording the pulsation was 6.22 times as sensitive as that used in standardizing (Fig. 4).

The error introduced by this simplification in the calculation of pulse volume is sufficiently small to be regarded as insignificant as far as this study is concerned. The following example is illustrative: J.G. (Fig. 7), a typical normal individual, had a maximal pulse deflection of 18 mm. at sensitivity 1 (15 cm. of water pressure) with the cuff inflated to 50 mm. Hg. By use of the Mariotte formula (including a conversion to centimeters of mercury pressure):

$$\frac{72 + 5 + (15 \div 13.6)}{72 + 5} = \frac{V}{V - 6}$$

$$V = 426 \text{ c.c.}$$

Using the figures for the pulsation itself,

$$\frac{72 + 5 + (1.2 \div 13.6)}{72 + 5} = \frac{426}{426 - v}$$

$$v = 0.48 \text{ c.c.}$$

Following nitroglycerin, the maximal pulse deflection became 26.5 mm. At a sensitivity of 3 this equals 1.75 cm. of water pressure. The standard deflection remains the same. Using the Mariotte formula, the pulse volume after nitroglycerin equals 0.71 c.c. Using the formula of a simple proportion:

$$Vp = \frac{6.00 \times 18}{34.5 \times 6.22} = 0.50 \text{ c.c. before nitroglycerin,}$$

and

$$Vp = \frac{6.00 \times 26.5}{34.5 \times 6.22} = 0.74 \text{ c.c. after nitroglycerin.}$$

The calculation by proportion provides a simple means to compare results in different subjects, or in the same subject at different times (e.g., in evaluating the effect of vasodilator drugs). The degree of accuracy is considered adequate for clinical studies of this nature.

The time elapse between the peak of the R wave (Lead I) of the electrocardiogram and the onset of the upstroke of the pulse wave was measured in all the subjects examined. There appeared to be no significant difference in the value of this time lapse for the normal group as compared to that of the groups with arterial or other diseases. The range and mean values for all three groups are nearly equal. It was observed, however, that no subject under 53 years of age, in this series, had a pulse transmission time of less than 0.20 sec. Nineteen subjects over that age, both in the normal and diseased groups, had shorter transmission times. In several cases of complete major artery obstruction, such as M.J. (Fig. 9), the transmission time on the obstructed side was longer than on the less involved leg.

The period of time between the onset of the upstroke to its highest point was determined in each case. There was no consistent relationship for this value to any particular group. This figure was most often 0.20 sec. or less. In many cases an accurate measurement could not be made due to the difficulty in determining the exact point of onset and the peak of the wave. Several abnormal forms had values well above 0.20 sec. (Fig. 9). There was a definite similar wave pattern seen consistently in the normals.

The response to nitroglycerin was varied. However, all showed some increase. Those normals showing little response to the drug may have received an inadequate dosage. These all occurred in the later part of the series when only 0.00025 Gm. was given. No absolute figure was found to distinguish the postnitroglycerin increase in pulse volume of the normals from that of the patients with arterial disease. There was an overlap of the range found in the two groups. The greater number of the normals showed a good response, even those of the older age group, while most patients with markedly symptomatic disease showed a poor response. This suggests that a small response to an adequate dose of nitroglycerin may indicate the presence of arterial disease. An overlap was also found in the range of values for size of the pulse waves before nitroglycerin in normal and diseased groups.

Abnormally shaped tracings were seen in most of the subjects known to have arterial disease. However, normally shaped tracings were seen in the presence of symptomatic disease.

The importance of standardization is shown by tracings made with cuffs applied to the ankle with different degrees of tightness. Table I illustrates the difference in the size of the deflections made by the same 6 c.c. standard in a pressure cuff applied snugly with a cloth band as compared to one fastened with metal rungs at three different degrees of tightness. Variations in the size of the limb examined make similar differences in sensitivity; thus findings in different subjects may not be comparable unless an adequate standardization is effected with each examination.

The great variety in size and shape of the index finger pulsations recorded by this method in both normal and diseased subjects prevents the drawing of any significant conclusions from these records. Records from the forearms were of interest only in those cases where a discrepancy existed between the two sides.

TABLE I. CHANGES IN AMPLITUDE OF STANDARD CONSEQUENT TO REDUCING CUFF TIGHTNESS

PRESSURE CUFF	VOLUME OF STANDARD (C.C.)	DEFLECTION OF STANDARD (MM.)
Cloth band type, tightly applied	6	34
Metal fastener type, tightly applied	6	31.5
Metal fastener type, tightness decreased, 1 metal rung	6	28
Metal fastener type, tightness decreased, an additional metal rung	6	23.5

SUMMARY

An analysis of the oscillograms (tracings of arterial oscillations) of the extremities of 127 subjects, both normal and diseased, is presented. Tracings were made with a specially constructed differential manometer based on the principles of the torsion-tension relationship of a twisted metal band, and utilizing an ordinary blood pressure cuff. An accurate standardization of the recordings was effected by use of a hypodermic syringe in the pneumatic system. Nitroglycerin was given as a test for vasodilatation. Records were taken with cuff pressure below the level of diastole, before and after medication. A consistent pattern was seen in the ankle oscillograms in the fifty-eight normal subjects studied. The patterns of tracings taken from the fingers and forearms were inconsistent and variable. Of forty-four patients with arterial disease, twenty-seven showed abnormally shaped pulse forms in ankle oscillograms. The remainder showed normally or equivocally shaped forms. A number of the twenty-five patients with various other diseases showed different degrees of abnormality, although most showed normal tracings. No absolute criteria as to timing and size of pulsations, or response to nitroglycerin, could be established, since there was a great overlap between the normal and diseased groups. A brief discussion of the principles involved is presented.

Although more accurate than the clinical determination of the oscillometric index, the oscillogram as recorded by this method is still of limited clinical value. The method promises to be of value in investigative work, by providing an objective measurement of the clinical evaluation of disease states of peripheral arteries, the effects of drugs, and the results of treatment. The manometer described may also be useful in other physiological and clinical studies.

SUMMARIO IN INTERLINGUA

Es presentate un analyse del oscillogramma arterial del extremitates de 69 patientes e 58 subjectos normal. Le methodo de registration e le apparatura empleate, includente un manometro de construction special, es describite in detalio. In le subjectos normal le oscillogrammas del cavilia exhibiva un configuration constante; illos del digitos e del antebracio esseva inconstante e variable. Inter 44 patientes con morbos arterial, 27 exhibiva anormalitates del forma de pulsation in lor oscillogrammas del cavilia. In le remanente 17 patientes de iste gruppo le correspondente configurationes esseva normal o equivoc. Inter le altere 25 patientes, qui habeva varie morbos non-arterial, alicunes monstrava configurationes con varie grados de anormalitate, sed in le majoritate del casos de iste gruppo le registrationes esseva normal.

Ben que nostre methodo oscillographic es plus exacte que le determination clinic del indice oscillometric, su valor clinic es ancora limitate. Nonobstante, illo pare promittente como medio de recerca.

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ACUTE HEMODYNAMIC EFFECTS OF HEXAMETHONIUM (C6) IN PATIENTS WITH EMPHYSEMATOUS PULMONARY HYPERTENSION

SALVATORE M. SANCETTA, M.D.

CLEVELAND, OHIO

WITH THE TECHNICAL ASSISTANCE OF GLADYS HECKMAN, R.N., AND HANNA JANOUSKOVEC, R.N.

THE eventual development of pulmonary hypertension which follows the progressive course of chronic pulmonary emphysema makes desirable the search for a chemical agent which would reduce pulmonary artery pressure. Ideally such an agent would effect a reduction of pulmonary arterial pressure and resistance, without detrimental hemodynamic alterations in the systemic circuit. In the case of the "blocking agents" now available, this would presuppose the possible existence of some extrinsic or intrinsic neurogenic control of pulmonary blood vessels.[2,5]

It was the purpose of these experiments to study the acute effects of intravenously administered hexamethonium (C6) on the systemic and pulmonary hemodynamics of emphysematous patients with established pulmonary hypertension in the horizontal position. The steady state[6] was maintained in all patients whose data are presented.

MATERIALS AND METHODS

Fifteen hospitalized adult male patients with well-established chronic pulmonary emphysema, ranging in age from 53 to 69 years, were studied by cardiac catheterization. The data for eight of the cases are reported; those for the remaining seven were discarded from the study, principally because of the failure to maintain the steady state throughout the entire experiment. Individuals were selected, insofar as possible, who had no associated cardiopulmonary complications at the time of study, in order to minimize the variations imposed by other alterations in organic state. Two patients had minor degrees of dry bronchiectasis, albeit clinically uninfected and radiologically unaccompanied by pulmonary fibrosis and pneumonitis. Mild right-sided failure in two patients was fully treated prior to catheterization, and none were anemic or polycythemic (hematocrit levels ranged from 38 to 47 per cent). None were either asthmatic or febrile. All subjects had clinical findings compatible with diffuse obstructive pulmonary emphysema, including reductions of more than

From the Department of Medicine of Western Reserve University at City Hospital, Cleveland, Ohio.
This investigation was supported by U. S. P. H. S. Grant No. H-1382.
Received for publication Oct. 12, 1954.

TABLE I. EFFECT OF C6 IN 8 PATIENTS WITH CHRONIC PULMONARY EMPHYSEMA AND PULMONARY HYPERTENSION (HORIZONTAL POSITION)
(MEAN PRESSURE IN PARENTHESES, PERCENTILE CHANGES IN ITALICS)

AGE AND BODY SURFACE			O_2CM /M²/MIN.		C. I. /M²/MIN.		H. R. /MIN.		B. A. P. MM. HG		P. A. P. MM. HG		PU. T. R. C. G. S.		E. T. P. R. C. G. S.		% ART. SAT.	
SK	62	C	143	%	3.78	%	103	%	139/72	(108.0)	28/14	(21.1)	307	%	1575	%	92.0	%
1.45	M²	C_6	134		2.86		94		79/46	(59.1)	22/10	(15.2)	293		1140		93.4	
				−6.3		*−24.3*		*− 8.7*		*− 45.8%*		*−28.0%*		*− 4.5*		*−27.6*		*+1.4*
HA	62	C	117		3.62		88		86/45	(66.0)	72/32	(47.3)	657		916		66.6	
1.60	M²	C_6	107		2.94		75		58/42	(47.0)	54/30	(42.0)	713		797		70.0	
				−8.6		*−18.8*		*−14.8*		*−28.8*		*−11.0*		*+ 8.5*		*−13.0*		*+3.4*
LP	54	C	122		2.39		115		99/69	(94.8)	32/16	(24.9)	595		2264		89.5	
1.40	M²	C_6	116		1.93		120		68/51	(62.1)	25/15	(20.2)	600		1713		88.3	
				−4.9		*−15.0*		*+ 4.3*		*−34.5*		*−19.0*		*+ 0.8*		*−24.4*		*+4.2*
WV	53	C	115		2.61		60		103/60	(77.2)	46/26	(34.6)	528		1180		83.1	
2.00	M²	C_6	109		2.26		83		81/56	(65.0)	39/23	(30.4)	538		1149		85.6	
				−5.2		*−13.4*		*+38.3*		*−15.9*		*−12.1*		*+ 1.8*		*− 2.6*		*+2.5*
AC	69	C	137		2.58		94		141/74	(102.0)	40/14	(25.4)	506		2033		88.9	
1.55	M²	C_6	126		2.36		91		112/65	(83.4)	34/15	(23.6)	514		1818		88.0	
				−8.0		*− 8.5*		*− 3.2*		*−18.2*		*− 7.1*		*+ 1.6*		*−15.0*		*−0.9*
AB	54	C	129		2.68		75		124/60	(82.8)	71/26	(43.0)	753		1451		80.4	
1.70	M²	C_6	117		2.19		60		92/47	(61.8)	64/22	(38.0)	831		1325		80.5	
				−9.3		*−18.3*		*−20.0*		*−25.4*		*−11.6*		*+10.3*		*− 8.7*		*+0.1*
JL	58	C	142		2.33		97		114/69	(87.0)	31/19	(26.8)	505		1641		81.4	
1.82	M²	C_6	132		1.91		86		86/54	(70.5)	31/19	(26.0)	597		1619		84.8	
				−7.0		*−18.0*		*−11.4*		*−19.0*		*− 3.0*		*+16.2*		*− 1.3*		*+3.4*
AA	69	C	138		3.67		75		81/48	(63.0)	39/14	(24.1)	332		869		84.5	
1.58	M²	C_6	136		3.20		75		60/36	(49.9)	29/12	(20.0)	316		805		84.5	
				−1.4		*−12.8*		*0*		*−28.0*		*−17.0*		*− 4.8*		*− 7.4*		*0*
Mean Percentile Change				*−6.3*		*−16.1*		*− 1.9*		*−26.9*		*−13.6*		*+ 3.7*		*−12.5*		*+1.7*

Key: O_2CM = oxygen consumption, C.I. = cardiac index, H.R. = heart rate, B.A.P. = brachial artery pressure, P.A.P. = pulmonary artery pressure, Pu.T.R. = pulmonary total resistance, E.T.P.R. = estimated total peripheral resistance, C = control, C6 = Hexamethonium.

35 per cent in vital and maximal breathing capacity, and no evidence of other coexisting heart disease. Catheterization criteria included the coexistence of pulmonary diastolic pressures above 10 mm. Hg, pulmonary total resistance of more than 260 c. g. s., and wedge pressure of less than 10 mm. Hg, when these values were the lowest for the first two and the highest for the last among several basal determinations in the same individual.

All observations were made with the subjects in the horizontal position. The data obtained in a previously reported series of ten normal control patients[10] were used for comparison. All subjects in the two groups were experimentally treated in the same fashion.

The day prior to cardiac catheterization, the patients were brought to the laboratory (constant ambient temperature 23 to 24° C.), and oxygen consumptions and arterial punctures done solely to acquaint the individuals with the experimental surroundings. Following overnight and morning sedation with phenobarbital (0.064 Gm.) and pentobarbital sodium (0.1 Gm.), cardiac catheterization was done according to the technique of Cournand and Ranges[3] employing standard 7F catheters. Right atrial, ventricular, pulmonary artery, wedge, and brachial artery pressures were transduced through Statham strain gauges and recorded on the Brush Multichannel Oscillograph. The zero point selected for intracardiac pressure determinations was uniformly 10 cm. anterior to the posterior surface of the thorax in the fourth intercostal space. Mean pressures were derived by planimetric integration of the pressure pulses inscribed in two consecutive, technically acceptable respiratory cycles.

Cardiac outputs were calculated by the direct Fick principle. Body oxygen consumptions were determined on four-minute samples collected in Douglas bags and analyzed on the Pauling Oxygen Analyzer, the final values being corrected to STP. Blood oxygen contents were determined on the Beckman D. U. spectrophotometer.[9] All determinations, including cardiac outputs, were done in duplicate. The data were discarded which showed more than 0.20 volumes per cent difference between duplicate samples for blood oxygen, more than 10 per cent variation between check cardiac outputs,[1] and more than 10 per cent difference among all oxygen consumptions[6] throughout the entire study.

Total pulmonary (Pu. T. R.) and estimated total peripheral (E. T. P. R.) resistances were calculated according to standard formulas[8] and expressed in centimeter-gram-second units. Of necessity, Pu. T. R. represents an approximation, since P_2 in the correct formula $(C \times (P_1 - P_2)/Q)$ must be assumed to be zero in the clinical formula.

Following the basal determinations, C6 was administered through the intracardiac catheter as previously described,[10] in a standard dose of 50 mg. during a 15 minute period. An additional 20 minutes were permitted to elapse for stabilization, and the determinations were repeated.

Attempts to study the effect of C6 during upright tilt in the pulmonary hypertensive patients were abandoned, after trials on three consecutive subjects had resulted in almost immediate loss of consciousness.

RESULTS

The data obtained in the eight emphysematous subjects are presented in Table I. The mean percentile changes, compared to those obtained in the previously reported group of ten normal control patients,[10] and analyzed statistically, (Fisher's '*t*' test), are presented in Table II. In addition, a similar analysis was carried out for several of the determinations in the group with emphysema.

There was a definite and constant decrease in the cardiac output. This decrease was statistically significant when compared to the control patients in whom no over-all change was noted ($p = 0.01$). This decrease in cardiac output occurred partly because, with the exception of two patients (W. V. and L. P.), there was no increase in heart rate. The behaviour of the heart rate is in direct contrast with the increase usually noted in normal patients and is statistically significant when compared to the latter ($p = 0.02$).

The brachial artery pressure decreased significantly in all instances ($p = 0.001$, not shown in Table II). There was no significant difference between the two groups.

TABLE II. COMPARISON OF CHANGES PRODUCED BY C6 ADMINISTRATION IN 10 NORMAL AND 8 EMPHYSEMATOUS PATIENTS IN THE HORIZONTAL POSITION (EXPRESSED AS MEAN PERCENTILE CHANGES)

	O_2CM /M^2/MIN.	C. I. /M^2/MIN.	H. R. /MIN.	B. A. P. MM. HG	P. A. P. MM. HG	PU. T. R. C. G. S.	E. T. P. R. C. G. S.	% ART. SAT.
N.	+1.7	+ 0.8	+19.1	−20.3	−17.3	+20.9	−17.0	+0.6
E.	−6.3	−16.1	− 1.9	−26.9	−13.6	+ 3.7	−12.5	+1.7
p	—	0.01	0.02	0.10	0.30	0.01	0.30	—

Mean pulmonary artery pressure decreased in all instances, but the decrease was predominantly in the systolic pressure, which decreased an average of 17.1 per cent, as against the diastolic, which showed an over-all decrease of 9.0 per cent. There was no significant difference in pressure decrease between the two groups. Of interest were the values for Pu. T. R. A significant decrease occurred in the normal subjects (more than 20 per cent), whereas no change was observed in the patients with emphysema. The difference between the two groups was statistically significant ($p = 0.01$). E. T. P. R. decreased in all instances. The decrease was of approximately the same order as in the control group.

There was no significant change in peripheral arterial oxygen saturations.

DISCUSSION

There is considerable controversy in the recently published literature regarding the existence of some neurogenic vasomotor control of the pulmonary bed during the basal resting state. The evidence for and against this has been reviewed by Cournand,[2] who favors a view against such participation. In addition it has been stated that C6 produces a decrease in brachial artery pres-

sure, at least in the systemically hypertensive patient not in failure, by reducing the cardiac output, and not primarily by decreasing peripheral resistance.[7] Both of these views will be examined in the light of the data which have been presented here.

The lung may be compared to a highly distensible "bag", wherein the resistance varies inversely with the volume blood flow.[4] In normal subjects, C6 lowers E. T. P. R. and brachial artery pressure. Principally by means of cardiac acceleration, the over-all venous return remains unaltered. Despite this constant pulmonary blood flow, there is a significant decrease in Pu. T. R. This points to a decrease in resistance elements in the lung, presumably vasomotor in nature. Whether this interruption occurs at the autonomic ganglionic level or by direct action on the vessel wall cannot be stated with absolute certainty initially. In the same fashion it may be stated that the over-all decrease in E. T. P. R. is brought about in a similar manner, and not as a result of blood pooling and a decrease in cardiac output, as is stated to occur in patients with essential hypertension not in failure.[7]

In patients with emphysema and pulmonary hypertension, there is a similar decrease in E. T. P. R. and in brachial artery pressure. In this case, however, there is no compensatory increase in heart rate, the reason for this being quite obscure. At least partly because of this lack in compensatory cardiac acceleration, there is a significant decrease in venous return, and, as would be expected, there is some decrease in pulmonary artery pressure. Under these circumstances, the pressure-flow load in the lungs is greatly reduced. This should result in retraction of distensible elements in the lungs, and a definite rise in pulmonary resistance. The fall in pulmonary artery pressure, however, is sufficiently great in comparison to the decrease in pulmonary flow that no change is noted in Pu. T. R. Apparently, something has occurred to counteract the increased pulmonary resistance expected with a decrease in flow, and it seems logical to conclude that, as in the case of normal subjects, this also represents a dilatation of pulmonary vasomotor elements.

In regard to the brachial artery pressure, it may likewise be stated that the decrease is logically due in part to interruption of vasomotor elements, and not to a decrease in cardiac output, since the decrease in brachial artery pressure appears to be disproportionate to the reduction in output.

C6 appears to be somewhat effective in reducing the elevated pulmonary artery pressure in patients with emphysema. From the clinical standpoint, however, this advantage is offset by the marked reduction in brachial artery pressure and cardiac output. In fact, the use of "blocking agents" such as C6 in these patients is not without danger, as borne out by the exaggerated orthostatic response to upright tilt which resulted in fainting when attempts were made to study the effects of standing. It is also worthy of mention that following the administration of C6, the decrease in brachial artery pressure can be totally abolished in the normal and almost totally in the emphysematous subject by 20 degree total head-down body tilt.[11] This occurs with no change in cardiac output from the levels observed in the horizontal position and is of practical value should it be desired to counteract an excessive decrease in blood pressure consequent to C6 administration in subjects such as the ones described.

SUMMARY AND CONCLUSIONS

1. The acute effects of intravenously administered hexamethonium have been investigated in eight subjects with uncomplicated pulmonary emphysematous hypertension. The data previously reported in ten normal control subjects served as controls.

2. Hexamethonium is effective in producing some reduction in pulmonary artery pressure in the emphysematous subject. Any advantage, however, is counteracted by a profound reduction in brachial artery pressure and venous return.

3. The data indicate that some neurogenic vasomotor control of pulmonary vessels exists in the basal resting state, and that hexamethonium is effective in interrupting this in both the normal and the emphysematous subject. The data do not indicate that an exaggerated degree of vasomotor tone capable of "blockade" at the autonomic ganglionic level exists in the emphysematous subject at rest.

SUMMARIO E CONCLUSIONES IN INTERLINGUA

Le acute effectos de hexamethonio in administration intravenose esseva investigate in octo patientes con non-complicate emphysematose hypertension pulmonar. Le previemente reportate datos in re dece casos normal serviva como controlo.

Hexamethonio es efficace in subjectos emphysematose in tanto que illo produce un certe reduction del pression pulmono-arterial. Iste beneficio, nonobstante, es neutralisate per un marcate reduction del pression brachio-arterial e del retorno venose.

Nostre datos indica que il existe in le stato de reposo basal un certe neurogene controlo vasomotor del vasos pulmonar e que hexamethonio es efficace in interrumper iste controlo in subjectos tanto emphysematose como etiam normal. Le datos non indica que il existe in le subjecto emphysematose in stato de reposo un exaggerate grado de tono vasomotor que esserea capace a producer un blocage per afficer le gangliones autonome.

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THE TRANSMISSION OF THE PULMONARY ARTERY PRESSURE ACROSS THE CAPILLARY BED OF THE LUNGS

GOFFREDO GENSINI, M.D.,* OSCAR J. BALCHUM, M.D., PH.D.,** AND S. GILBERT BLOUNT, JR., M.D.

DENVER, COLO.

INTRODUCTION

THE technique for obtaining wedged pressures from the pulmonary artery and pulmonary veins was first described by Hellems and associates in both experimental animals[1] and in man.[2] Calazel and co-workers[3] obtained venous wedged pressures in two patients with atrial septal defects. They found that the mean pulmonary venous pressure levels were approximately the same as the mean pulmonary arterial pressures, but no observations were made in regard to their contours.

Since then considerable clinical and experimental work has been done in the attempt to ascertain the meaning of the designation pulmonary "capillary" pressure, also referred to as the pulmonary artery wedged pressure. It is the consensus that the pulmonary artery wedged pressure (PVWP) reflects the pressure level within the left atrium rather than being a measure of the true pulmonary "capillary" pressure.[4,5] Several investigators,[6,7] however, have demonstrated that there is a close similarity between the left atrial and the pulmonary artery wedged pressure contours. Mueller and associates[8] have shown that in the dog at low left atrial pressure levels there was no similarity in contour; however, at levels higher than 35 mm. Hg a striking similarity in both contour and level was present.

Recently, Weissel and associates[9] reported the recording of pulmonary venous wedged pressure (which they termed pulmonary capillary arterial pressure) in patients with atrial septal defects. They stressed that, although there was no relationship as to either level or contour between PVWP and pulmonary artery pressure, the PVWP did resemble an arterial pulsation. Wood[10] mentioned that the pulmonary artery pressure in patients with atrial septal defects and high pulmonary blood flows could be obtained by introducing a catheter into a pulmonary vein and wedging it into a branch of the vessel. He considered that this was dependent upon the dilatation of the pulmonary vascular bed secondary to the high pulmonary artery blood flows in patients with normal or

From the Cardiovascular Laboratory, Department of Medicine, University of Colorado School of Medicine, Denver, Colo.

This study was supported by United States Public Health Service Grant H-1208.

Received for publication Oct. 18, 1954.

*Research Fellow, Colorado Heart Association.

**Research Fellow, American Heart Association.

TABLE I. HEMODYNAMIC FINDINGS OF GROUPS A AND B

GROUP	PATIENT AGE	PULMONARY ARTERY PRESSURE (MM. HG)	PULMONARY VENOUS WEDGED PRESSURE (MM. HG)	PULMONARY ARTERY WEDGED PRESSURE (MM. HG)	PULMONARY BLOOD FLOW (L./MIN.)	PULMONARY INDEX (L./MIN./M.^{2})	TOTAL PULMONARY RESISTANCE (DYNES/SEC./CM.$^{-5}$)	DIAGNOSIS
A	J. C. 5 yr.	30/8	33/17	3/–2	5.44	6.90	221	Atrial septal defect
Increased pulmonary blood flow and normal total pulmonary resistance	D. G. 8 yr.	30/12	31/7	10/–1	5.85	5.90	245	Anomalous pulmonary veins entering the right atrium
	A. H. 7 yr.	31/10	31/9	9	9.01	11.25	168	Anomalous pulmonary veins entering the right atrium
B	D. B. 3 yr.							Valvular pulmonary stenosis with patent foramen ovale
Normal pulmonary flow and increased total pulmonary resistance	Pre-op.	16/8	30/14	6	2.38	4.11	403	
	Post-op.	41/18	42/22		3.60	7.20	549	

decreased pulmonary vascular resistance, or indeed in any instance where the pulmonary resistance is normal or low.[11] Wilson and associates[4] in an extensive study reported that the PVWP contour did not resemble that of the pulmonary artery pressure, although the mean pressures were nearly the same.

The present study reports on the relationship between the PVWP and the pulmonary artery pressure contours in the attempt to determine whether undamped transmission of pulmonary artery pressure pulses takes place and can be recorded.

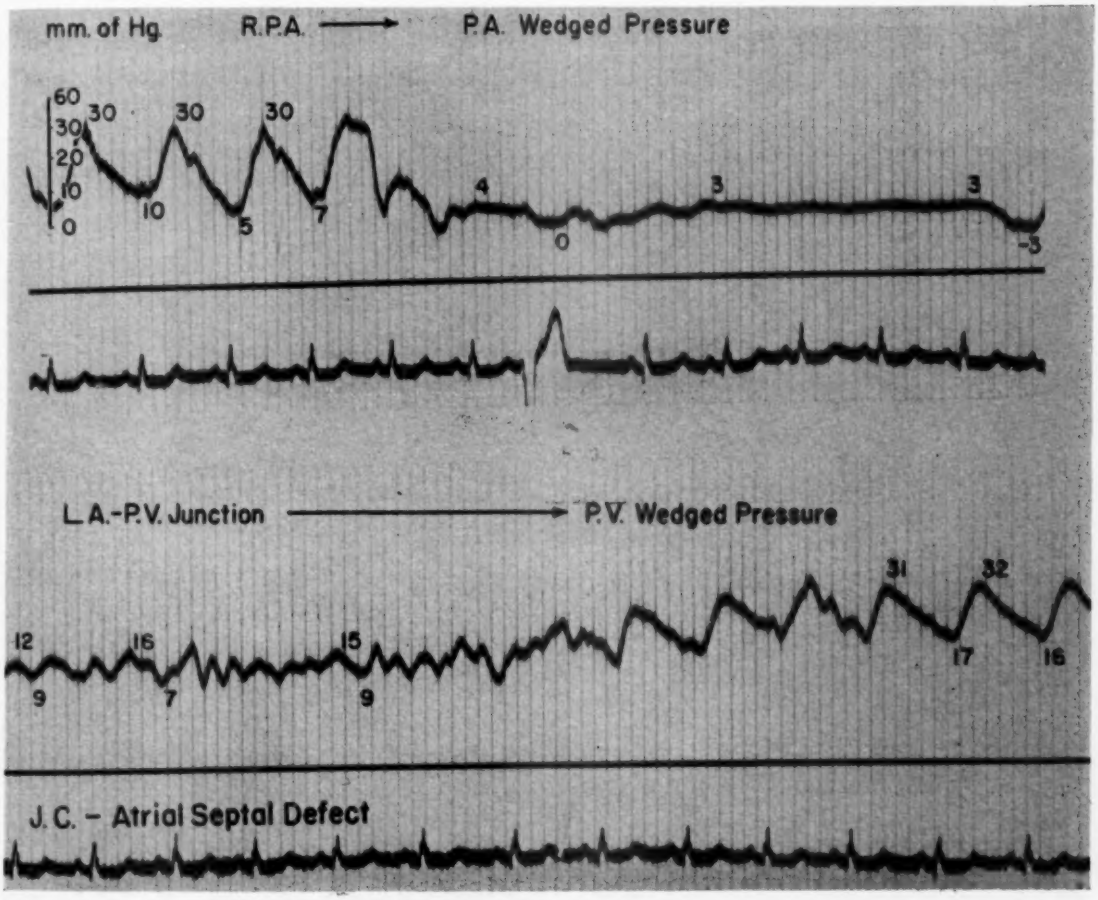


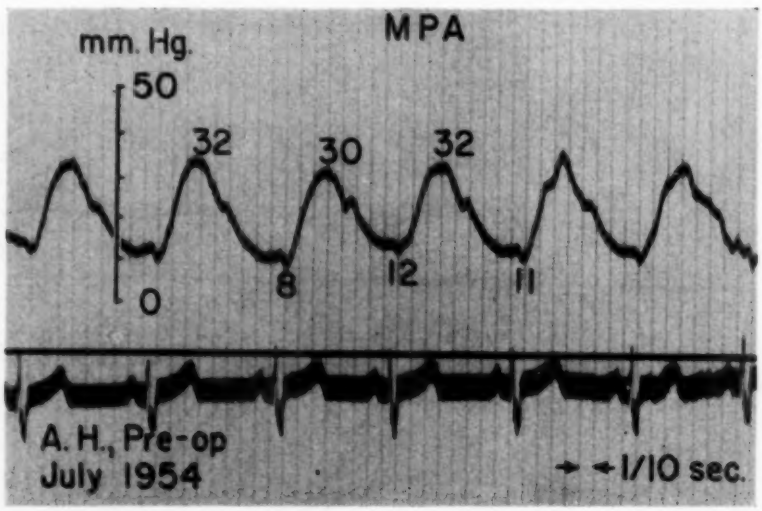
Fig. 1.—Upper part: The right pulmonary artery pressure and the pulmonary artery wedged pressure. Lower part: The left atrial-pulmonary venous pressures and the pulmonary venous wedged pressure (J. C., atrial septal defect, Group A).

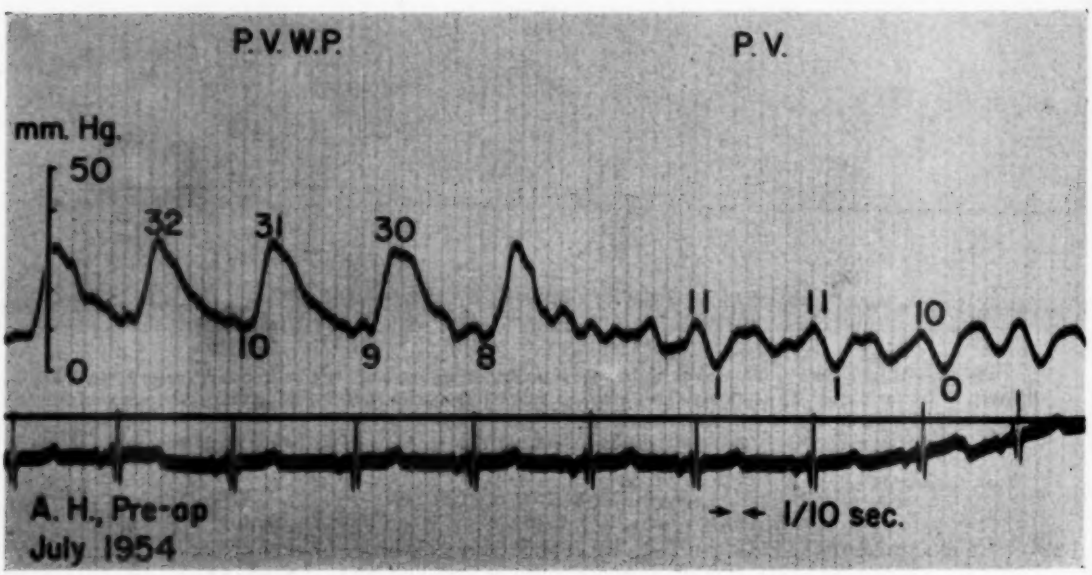
MATERIAL AND METHODS

Two patients (D. G. and A. H.) with anomalous connections of pulmonary veins to the right atrium, three patients (J. C., M. S., and R. H.) with atrial septal defects, and one patient (D. B.) with valvular pulmonic stenosis and patent foramen ovale were the subjects of this study.

Cardiac catheterization was performed according to the usual methods, using a number 7F Cournand catheter (with the opening at the tip). Once the pulmonary artery and the pulmonary artery wedged pressures were obtained, the catheter was withdrawn into the right atrium and then introduced through the defect or the patent foramen ovale into the left atrium and then wedged into a small branch of a pulmonary vein. The recording of the various pressures was not simultaneous; however, the measurements were carried out in rapid

A.





B.

Fig. 2.—*A*, The main pulmonary artery pressure. *B*, The pulmonary venous wedged pressure and pulmonary venous pressures. (A. H., anomalous connection of pulmonary veins to the right atrium, Group A).

succession. In every case that it was possible to enter a pulmonary vein, the PVWP was easily obtained by advancing the catheter as far as it would go into a branch of the vein. Pressure tracings were continuously recorded during the withdrawing of the catheter from a wedged venous position to the right atrium. This procedure was repeated several times, with identical results.

The pressures were recorded by means of Statham strain gauges and a Hathaway oscillographic camera. The reference point was 10 cm. above the patient's back when the body weight was above 20 kilograms, and 5 cm. above the back when the weight was less than 20 kilograms. The cardiac output was calculated according to the Fick principle. The Van Slyke technique was used in the analysis of the oxygen content of the blood samples, and the Scholander micromethod was used for the determination of the oxygen content of the expired air.

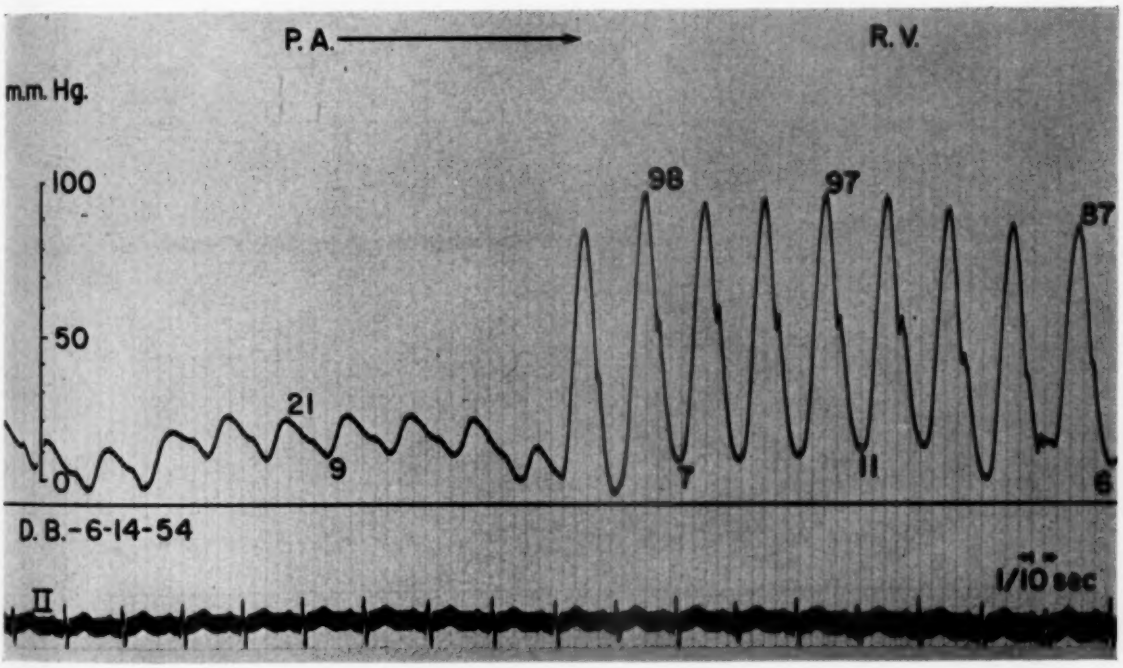


Fig. 3.—Pulmonary artery and right ventricular pressure in D. B. (Preoperative valvular pulmonic stenosis and patent foramen ovale; Group B).

RESULTS

A. The Pulmonary Venous Wedged Pressure In Patients With Increased Pulmonary Blood Flows And Normal Total Pulmonary Resistances.—There were three patients in this group (J. C., D. G., and A. H.). The contours and pressure levels of the pulmonary artery pressure and the PVWP corresponded very closely (Table I, Fig. 1). In J. C. the pulmonary artery diastolic pressure was lower than the diastolic PVWP, but the systolic pressures were almost the same. In D. G. the diastolic PVWP was lower than that of the pulmonary artery, but the systolic pressures were the same. In A. H. the pressure levels were equal and the contours resembled each other very closely (Fig. 2, *A* and *B*).

B. The PVWP In Patients With Normal Pulmonary Blood Flows And Increased Total Pulmonary Resistance.—The patient in this group (D. B.) had pulmonic valvular stenosis with patent foramen ovale and was studied before and after pulmonary valvulotomy. Before operation the pulmonary artery pressure was low, averaging 16/8 mm. Hg (Table I, Fig. 3), whereas the PVWP was 30/14 mm. Hg (Fig. 4). The PVWP and the pulmonary artery pressure contours had similar wave forms. The contours of the pulmonary venous and left atrial pressure were definitely different from those of the PVWP.

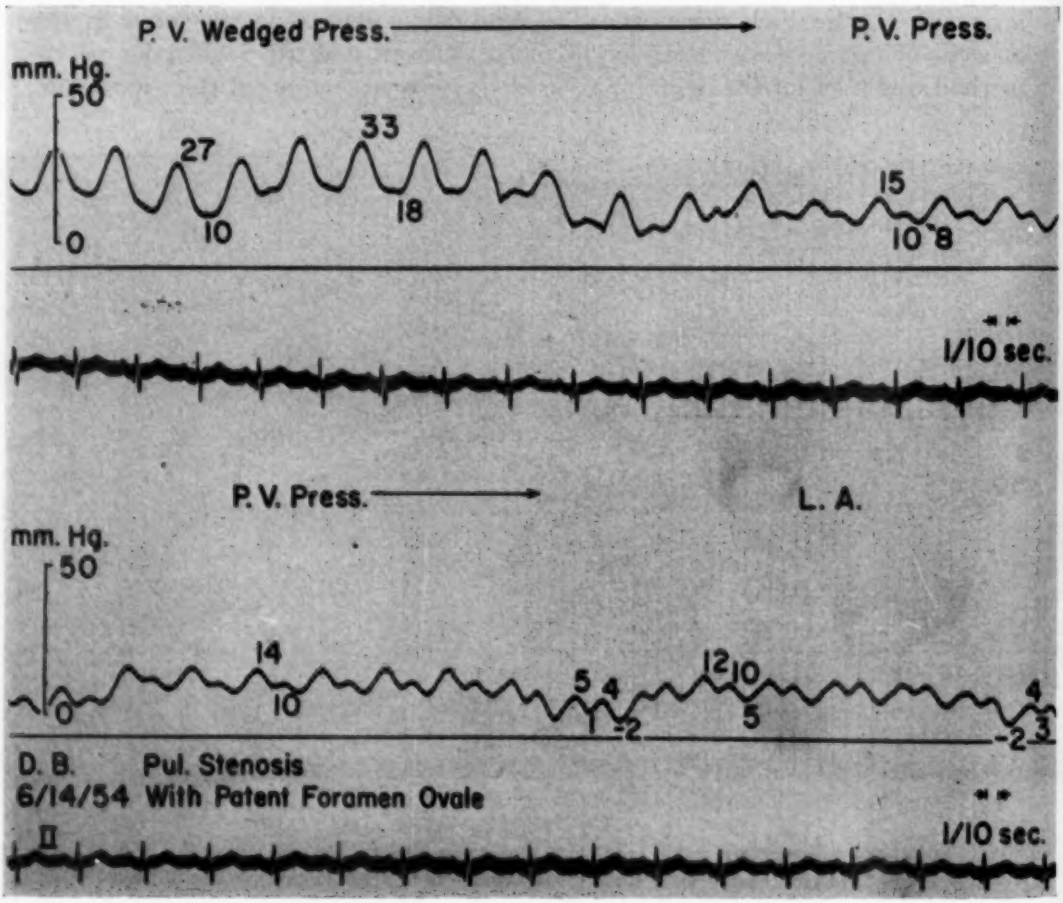


Fig. 4.—Upper part: Pulmonary venous wedged pressure and pulmonary venous pressure. Lower part: Pulmonary venous pressure and left atrial pressure. (D. B., preoperative, valvular pulmonic stenosis and patent foramen ovale; Group B).

After operation the pulmonary artery pressure was 41/18 mm. Hg, and the PVWP was almost the same, being 42/22 mm. Hg (Fig. 5). The pulmonary artery blood flow and resistance were increased above the preoperative levels. It will be noticed that prior to surgery the PVWP was higher than the pulmonary artery pressure, whereas after the valvulotomy they were the same. The factors determining this phenomenon will be discussed later.

In addition there were two patients with atrial septal defects (M. S. and R. H.) in whom the PVWP was measured; however, the pulmonary artery was not intubated in these patients. The contours of the PVWP obtained closely resembled those of a pulmonary artery pressure. The PVWP in the first patient measured 39/16 mm. Hg, and in the second patient it averaged 23/9 mm. Hg.

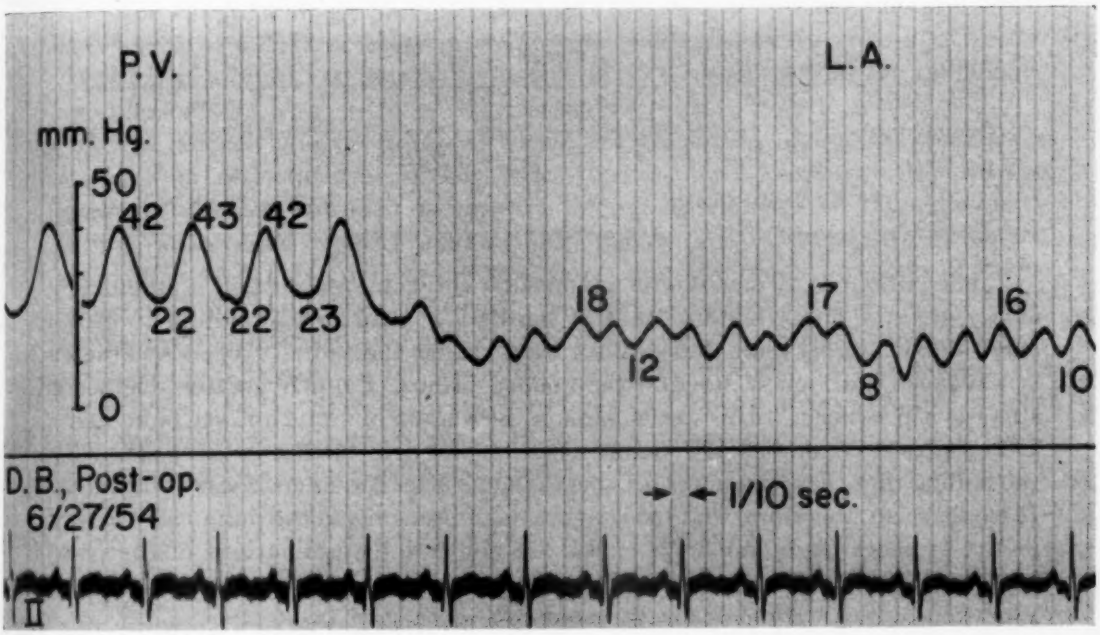


Fig. 5.—Pulmonary venous wedged pressure and left atrial pressure in D. B. after pulmonic valvulotomy.

DISCUSSION

The contour of the PVWP resembled that of a pulmonary artery pressure wave form without exception in these six patients. This has been mentioned before by Wood[10]; however, others have not reported this observation.[3,4]

The wave form of the PVWP consists of a rapidly ascending limb; the time from the onset to the peak of the pressure pulse in J. C. being 0.2 sec., with an identical value in the pulmonary artery. The fall in pressure is equally rapid in both the pulmonary artery and PVWP, as can be seen by comparing the descending limbs of the pressure pulses (Fig. 1).

The time delay from the peak of the QRS complex to the beginning of the pressure pulse is less in the pulmonary artery than in the PVWP in all three patients in group A (Table II). Since the pulse wave must traverse the pulmonary vascular bed, this delay is to be expected. This time delay of pressure pulses traveling across the pulmonary vascular bed has been previously noted.[8,9]

TABLE II. COMPARISON BETWEEN TIME DELAYS FROM PEAK OF QRS COMPLEX TO BEGINNING OF PRESSURE PULSE OF PULMONARY ARTERY AND PULMONARY VENOUS WEDGED PRESSURE

GROUP	PATIENT	TIME FROM PEAK OF QRS TO ONSET OF PULMONARY ARTERY PULSE PRESSURE (SEC.)	TIME FROM PEAK OF QRS TO ONSET OF PULMONARY VENOUS PRESSURE PULSE (SEC.)
A	J. C.	0.09	0.13
	D. G.	0.05	0.11
	A. H.	0.05	0.09
B	D. B.		
	Pre-op.	0.20	0.12
	Post-op.	0.06	0.10

The patient in Group B with pulmonary valvular stenosis had a pulmonary artery pressure about one-half that of the PVWP prior to valvulotomy. However, following operation these values were almost the same. When a catheter is advanced through a stenotic pulmonary orifice, a much greater degree of stenosis is produced. This would explain the finding of a much lower pulmonary artery pressure than PVWP before operation and is further substantiated by the finding that these pressures became the same after the stenosis was obliterated. It would seem, therefore, that measurements of pressures in the pulmonary artery in the presence of pulmonary stenosis are not true determinations of the pressures existing within the vessel, since an increased degree of stenosis has been produced by the method of measurement.

In the light of these findings, the pulmonary artery pressure in pulmonary stenosis must be higher than previously thought. The contours and levels of the pulmonary artery pressure heretofore have been used as a gauge of the degree of stenosis. This method of analysis must be used cautiously, as the damping effect of the catheter in a stenosed pulmonary orifice will increase rapidly as the degree of stenosis increases. From our findings the damping effect of the catheter in a normal or only slightly stenosed pulmonary orifice (as after pulmonary valvulotomy) is not measureable. In these latter instances the PVWP and pulmonary artery pressure were about the same (Table I).

The damping effect of the presence of a cardiac catheter in a narrowed pulmonary valve orifice can also be appreciated by consideration of the time delays (D. B., Table II). The time from the onset of electrical systole to the onset of the pressure pulse in patient D. B. was much greater in the pulmonary artery than in the PVWP before operation. The opposite was found to be true following the obliteration of the stenosis. After surgical relief of the stenosis in D. B these values became similar to those present in the three patients in Group A with normal pulmonary valves.

The magnitude of the total pulmonary resistance and of the pulmonary blood flow could be factors which might affect the wave form, the level, and the time of onset of the pressure pulses. Within the range of our data, however,

total pulmonary resistance seems to have but slight effect on the transmission of the pulmonary arterial pressure pulses across the pulmonary vascular tree. In patient D. B. (Table I), postoperatively the pulmonary vascular resistance was twice that of normal (J. C., D. G., A. H.) and yet the pressure contours and levels of the pulmonary artery were faithfully reflected in the PVWP. It might be expected that when the resistance becomes greatly elevated the wave form would be altered.

The range of magnitude of pulmonary blood flow in these cases is small, and normal as well as increased pulmonary flows do not seem to affect significantly the transmission of the pulmonary artery cyclic pressure across the pulmonary vascular bed.

The wedged pressure obtained within the pulmonary artery has come to be regarded as an estimation of left atrial pressure level,[3-6] whereas the wedged pressure obtained within a pulmonary vein is a reflection of the pulmonary artery pressure, as demonstrated by this study. We would like to stress the point brought out by Wilson and associates[4] that the present method of calculating the pulmonary arteriolar resistance is but a determination of the resistance of the total pulmonary vasculature. This is so because the pressure gradient between the pulmonary artery pressure and the pulmonary "capillary" pressure is equivalent to the drop in pressure between pulmonary artery and left atrium and not from the pulmonary artery to the pulmonary capillaries, as no method of measuring true pulmonary capillary pressure exists at the moment.

SUMMARY AND CONCLUSIONS

1. The relationship of the wave forms and pressure levels of the PVWP and pulmonary artery pressure have been compared in four patients, and the PVWP analyzed in six patients.

2. The PVWP was easily obtained in all six instances and closely resembled a pulmonary artery pressure pulse. Where comparison was possible the pressure levels and contours of the PVWP were very similar to the pulmonary artery pressure levels and contours in the same patients.

3. The resistance of the pulmonary vasculature and the magnitude of the pulmonary blood flow apparently had little effect upon the transmission of the pulmonary artery pressure within the limits of this study.

4. In pulmonary valvular stenosis the PVWP is greater than the pulmonary artery pressure. This is due to the greater degree of stenosis that exists when the cardiac catheter is present in an already stenotic pulmonary valvular orifice. Therefore, it would appear that the PVWP is a more accurate estimation of the pressure actually existing in the pulmonary artery in the case of pulmonic stenosis.

5. The effect of the pulmonary valve stenosis on the time of onset of the pressure pulses in the pulmonary artery and PVWP has been observed and compared to that of patients with normal pulmonary valves.

6. The fallacy in the customary calculation of the pulmonary arteriolar resistance has again been emphasized.

SUMMARIO IN INTERLINGUA

Cuneate pressiones pulmono-venose esseva registrate ab 6 patientes, includente 3 con defectos del septo atrial e 2 con connexiones anormal inter le venas pulmonar e le atrio dextere. Le sexte patiente, con isolate stenosis valvulo-pulmonic e un patente foramine oval, esseva studiate tanto ante como etiam post valvulotomia. Le characteristicas del cuneate pressiones pulmono-venose esseva comparate con illos del pressiones pulmono-arterial. Similaritates inter le duo esseva constatate. Le mechanismo e le interpretation de iste constatationes es discutite.

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THE FORMATION OF EDEMA AND THE EFFECT OF SODIUM ON COLLOID OSMOTIC PRESSURE

RUSSELL H. KESSELMAN, M.D.

PHILADELPHIA, PA.

IT IS generally agreed that sodium metabolism plays an important role in the mechanism of edema formation. This may include edema caused by cardiac, renal, or hepatic disease. The essential problem has been considered to be a metabolic state in which there is an abnormal retention of salt, in consequence of which water is retained and edema may develop.

The dynamics of the action of salt retention on the distribution of fluids in the different body fluid compartments is not often rigorously examined. An attempt will be made to show the operation of one mechanism having some control over the exchange of fluid between blood plasma and interstitial fluid. Primarily, consideration will be given to the relationship between electrolyte concentration and colloid osmotic pressure. This has had some previous examination.[1,2] Undoubtedly many other mechanisms for the discussed fluid shifts are operative, and the present study will only attempt to elucidate one of these, the relative importance of which is difficult to determine. The approach is to rely on established concepts of physical chemistry, but to use at present certain simplifying abstractions which will permit an adequate adherence to the orders of magnitude existing in the factors examined but not make the discussion impossibly cumbersome.

The usual equation for calculating the osmotic pressure of a solution[3] is:

$$\pi = CRT \qquad (1)$$

in which π is the osmotic pressure, T is the absolute temperature, R is the ideal gas constant, and C is the concentration of the solution in moles of solute per liter of solution.

Capillary endothelium is a dialyzing membrane permeable to ordinary crystalloidal ions but not to colloids or their ions. Within the capillary is blood plasma and outside of it is interstitial fluid. The predominant cation in plasma and interstitial fluid is the Na^+ ion and the predominant anions in plasma are Cl^-, HCO_3^-, and plasma protein.[4] The anions to be considered in interstitial fluid include only HCO_3^- and Cl^-, protein being omitted here because of its negligible concentration.

The symbols y + z and y, respectively, represent the cation concentration and the nonprotein anion concentration in blood plasma. The concentrations of the anions and the cations will be considered to be equal in interstitial fluid, and consequently the same symbol x is used to represent either of these con-

From the Department of Medicine, Woman's Medical College of Pennsylvania, Philadelphia, Pa.
Present address: Mount Sinai Hospital, New York, N. Y.
Received for publication Oct. 18, 1954.

centrations. The normality of plasma protein is z, n is its valence, and z/n must be its concentration in moles of protein per liter of solution. It is evident that the osmotic pressure of the blood plasma may be given by

$$\pi_b = RT(z + z/n + 2y) \tag{2}$$

and that the osmotic pressure of interstitial fluid may be given by

$$\pi_i = 2xRT.$$

According to the Donnan equilibrium[5] relation

$$x^2 = y(y + z). \tag{3}$$

The observed pressure of equilibrium, P, is the difference between the osmotic pressures of the two solutions ($\pi_b - \pi_i$) and is given by[3]

$$P = RT(z + z/n + 2y - 2x). \tag{4}$$

P represents what is generally referred to by physiologists as colloid osmotic pressure. By putting the expression for x obtained from equation (3) into equation (4), it is found that

$$P = RT[z + z/n + 2y - 2\sqrt{y(y + z)}\,]. \tag{5}$$

The relationship will be obtained that exists between the colloid osmotic pressure across capillary endothelium and the plasma sodium concentration when the other variables affecting the colloid osmotic pressure are maintained at any constant levels. The following normal numerical values will be used in studying the relationship of P and $[Na^+]$, the plasma sodium concentration:

$R = (0.849 \text{ liter} - \text{mm } H_2O)/\{\text{millimole} - (°C. + 273)\}$,
$T = 37°C. + 273$,
$z = 16$ milliequivalents/liter at physiologic pH's,
concentration of plasma albumin = 46,000 mg./liter,
concentration of plasma globulin = 22,000 mg./liter,
molecular weight of plasma albumin = 70,000, and
molecular weight of plasma globulin = 165,000.

Since $y + z$ has been defined as the cation concentration in plasma and since Na^+ is the predominant cation in plasma, it can be stated that

$$\begin{aligned} [Na^+] &= y + z, \\ &= y + 16, \text{ or} \\ y &= [Na^+] - 16. \end{aligned}$$

Substituting the foregoing data into equation (5), term by term, and using Dalton's law of partial pressures for albumin and globulin, we have

$$\begin{aligned} P = 0.849(310)[16 &+ 46{,}000/70{,}000 + 22{,}000/165{,}000 \\ &+ 2([Na^+] - 16) - 2\sqrt{([Na^+] - 16)\{([Na^+] - 16) + 16\}}\,]. \end{aligned} \tag{6}$$

Simplifying, there is obtained

$$P = 263\left\{2\,[Na^+] - 15.21 - 2\sqrt{[Na^+]\,([Na^+] - 16)}\right\}. \tag{7}$$

Instead of substituting $([Na^+] - 16)$ for y in equation (4), we could have just as readily substituted $([HCO_3^-] + [Cl^-])$, the sum of the plasma concentrations of bicarbonate and chloride. The graph of equation (7) is plotted in Fig. 1.

Calculated values of P are given in the figure for the variations of plasma sodium concentration within the most extreme limits.

DISCUSSION

Examination of Fig. 1 and consideration of the method of derivation of the equation from which the graph is drawn reveal that, when the character and quantity of plasma protein and the plasma pH are kept constant, a fall in plasma sodium concentration produces a rise in plasma colloid osmotic pressure. (It should be remembered that with the diminution of plasma sodium there will of course be an associated fall in the diffusible anions, mainly Cl^- and HCO_3^-.)

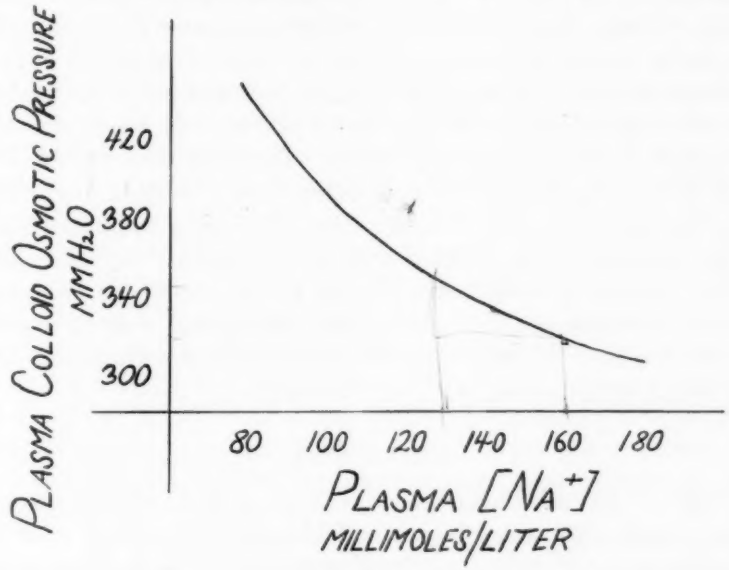

Fig. 1.

P could actually be graphed as a function of $[Na^+]$ for any values of plasma albumin and plasma globulin chosen with increases in plasma proteins obviously elevating the level of P. Using values of the plasma proteins different from those used in deriving equation (7) would lead to constants other than the 15.21 and the 16 being used there. It should be understood that these equations have been derived for idealized conditions and that consideration of factors influencing colloid osmotic pressure in a lesser order of magnitude has been omitted. Consequently equation (7) is to be regarded as semiquantitative, although for physiologic purposes it is quite descriptive of the relationship between P and $[Na^+]$ and gives a good representation of the orders of magnitude of P as a function of those of $[Na^+]$.

Osmotic pressure of body fluids is undoubtedly a very important factor in influencing shifts of fluid between the different body fluid compartments. The demonstration that a fall in plasma sodium concentration produces a rise in plasma colloid osmotic pressure and that a rise in plasma sodium concentration produces a fall in plasma colloid osmotic pressure gives valuable insight into one of the mechanisms of how levels of electrolytes in plasma and in interstitial

fluid will influence the quantity of fluid in these compartments. Edema formation would be favored by an elevation of plasma sodium, and edema resorption would be favored by a lowered plasma sodium. This is in agreement with observations of the role of increased and decreased sodium intake and output in many edematous states observed clinically.

It might be argued that wide shifts in serum sodium concentration are not ordinarily seen in instances such as the successful treatment of the edema of congestive heart failure with low-sodium diets, ion exchange resins, or mercurial diuretics. A reduction in plasma sodium level of 10 millimoles per liter (as from 145 millimoles per liter to 135 millimoles per liter) will raise plasma colloid osmotic pressure by 10 mm. of water, an amount which could very well result in major shifts of body fluid. Another and perhaps more important reason why wider shifts in serum sodium concentration are not observed is that the body fluid compartments are in a state where they are close to if not at equilibrium with each other and are in no way closed systems. Of particular importance in this connection is the role of the kidney. To make this clearer, it would be well to think of the situation where a small amount of sodium might be removed or lost from the plasma. The concentration of plasma sodium would then be lower and the plasma colloid osmotic pressure would be elevated. Fluid would shift from the interstitial fluid compartment to the intravascular compartment (plasma). The kidneys might rapidly move additional water from the plasma to elevate the lowered plasma sodium concentration. However, the precise sequence of events is, of course, really not known.

CONCLUSIONS

On the basis of physico-chemical considerations depression of plasma sodium level has been shown to raise plasma colloid osmotic pressure and vice versa. This is an important controlling mechanism over the distribution of fluid in the intravascular and interstitial fluid compartments. An important relationship of sodium metabolism to edematous states is thereby furnished.

CONCLUSIONES IN INTERLINGUA

Super le base de considerationes physico-chimic nos ha demonstrate que le depression del nivello del natrium del plasma augmenta le colloide pression osmotic del plasma e vice versa. Isto representa de un latere un importante mechanismo regulatori pro le distribution de fluido in le compartimentos intravascular e interstitial; del altere latere illo revela un importante relation inter le metabolismo de natrium e statos edematose.

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ON THE RECOGNITION AND SIGNIFICANCE OF PLEURAL LYMPHATIC DILATATION

BERTRAM LEVIN, M.D.*

CHICAGO, ILL.

THE pathologic changes in lungs of persons suffering from mitral valvular disease have been extensively written about and are well known. However, the alveolar septal thickening, the medial hypertrophy of the arteries, and the chronic passive congestion do not account for a finding frequently present in the chest roentgenograms of persons with mitral stenosis. This consists of short transverse lines in the bases of the lungs, approximately two to three centimeters long, extending outward to the pleural surfaces (Fig. 1). The lines are arranged in parallel fashion, one above the other. They are confined to the lung bases, usually bilateral but occasionally unilateral, occurring with equal frequency in both lungs. Only rarely is the finding present above the midportion of the lung fields. These transverse linear streaks, when present, are almost always seen in the posteroanterior film; occasionally they are best demonstrated or seen only in the oblique projection; and only rarely are they evident in the lateral view.

In their textbook of x-ray diagnosis Shanks and Kerley[1] call attention to these basal pulmonary lines as seen in silicosis. They attribute these markings to dilated intercommunicating pleural lymphatics. In discussing the roentgenographic findings in heart failure, they also note that intercommunicating lymphatics are often clearly visible. In some of their published illustrations of mitral stenosis these markings are strikingly prominent although they are not described in the text.

Davies and associates[2] noted that these basal striae were evident in ten of fifty-one cases with pulmonary hypertension of varying severity in patients with mitral stenosis. The pulmonary artery pressures of these cases were not stated. In a recent report on mitral valve disease Steiner and Goodwin[3] call attention to horizontal linear shadows in the lower zones of the lungs, most marked in patients with pulmonary hypertension and congestive heart failure. The authors offer no explanation for these lines.

From the Department of Diagnostic Roentgenology, Michael Reese Hospital, Chicago, Ill.
Received for publication Oct. 21, 1954.

*This study was made while a Fellow of The American Heart Institute, Variety Club Heart Hospital, University of Minnesota Hospitals, Minneapolis, Minn.

Recently Whitaker and Lodge,[4] in a paper discussing the radiologic manifestations of pulmonary hypertension in patients with mitral stenosis, noted the appearance of the basal horizontal lines. They did not attempt to account for the lines but did state that they are a sign of moderate or severe pulmonary hypertension.

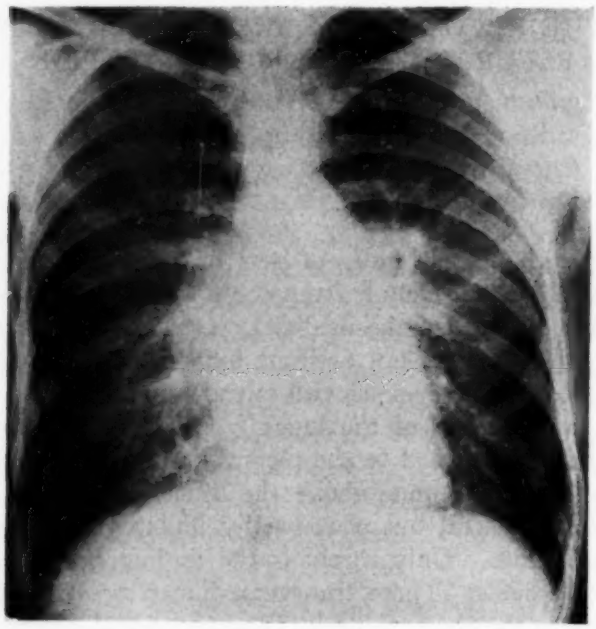


Fig. 1A.—F. M., 22-year-old male suffering from mitral stenosis. Mean pulmonary artery pressure, 57 mm. Hg.

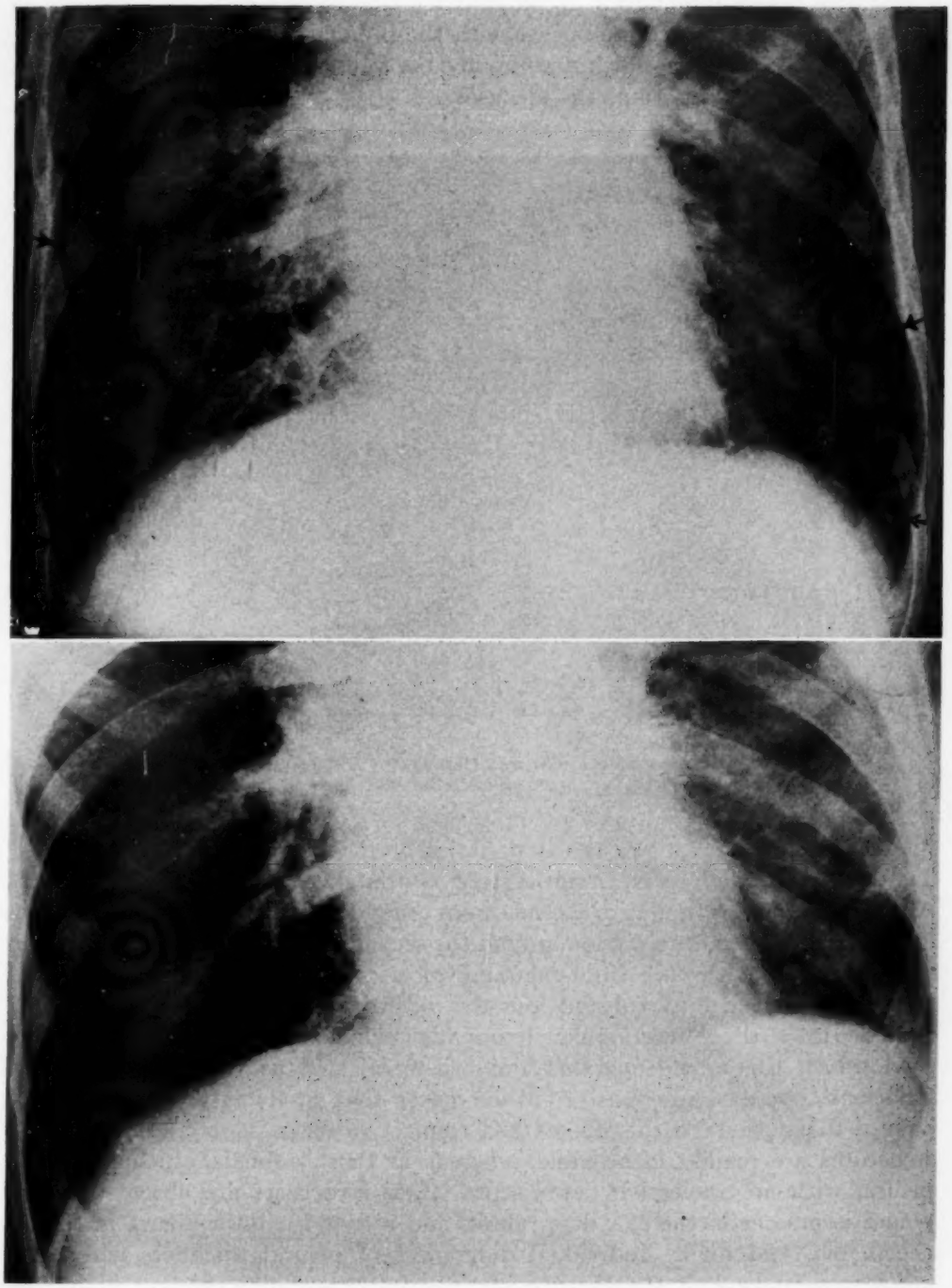
Fleischner and Reiner[5] have also reported on the linear horizontal shadows in the lung bases of patients suffering from either acute or chronic recurrent pulmonary congestion, particularly in severe mitral stenosis. They attribute these shadows to three factors: the intraseptal deposition of hemosiderin, the paraseptal accumulation of hemosiderin macrophages, and the intensity difference of septal-paraseptal bands on the one hand and the hemosiderin deposition in the lung lobules, as a whole, on the other. These authors have noted the fleeting character of these linear shadows in some cases. In these instances they attribute these lines to edematous widening of the interlobular septa due to absorption of edema fluid.

This report is submitted in an attempt to further the recognition of and to discuss the possible significance of transverse basal pulmonary striae.

ANATOMIC CONSIDERATIONS

The pulmonary arteries are enmeshed in a network of accompanying lymphatics which communicate with the bronchial lymphatics at the site of bronchial bifurcations.[6] Lymphatics are also intimately associated with the pulmonary veins. The smaller veins may be accompanied by only one or two lymphatics,

B.



C.

Fig. 1.—*B* and *C*. F. M., same as Fig. 1*A*. *B*, Jan. 2, 1953. There is marked dilatation of basal pleural lymphatics manifested on the roentgenogram as parallel transverse lines in both lung bases (arrows). *C*, March 12, 1953. The basal striae are no longer evident. Mitral valvulotomy had been performed on Jan. 29, 1953.

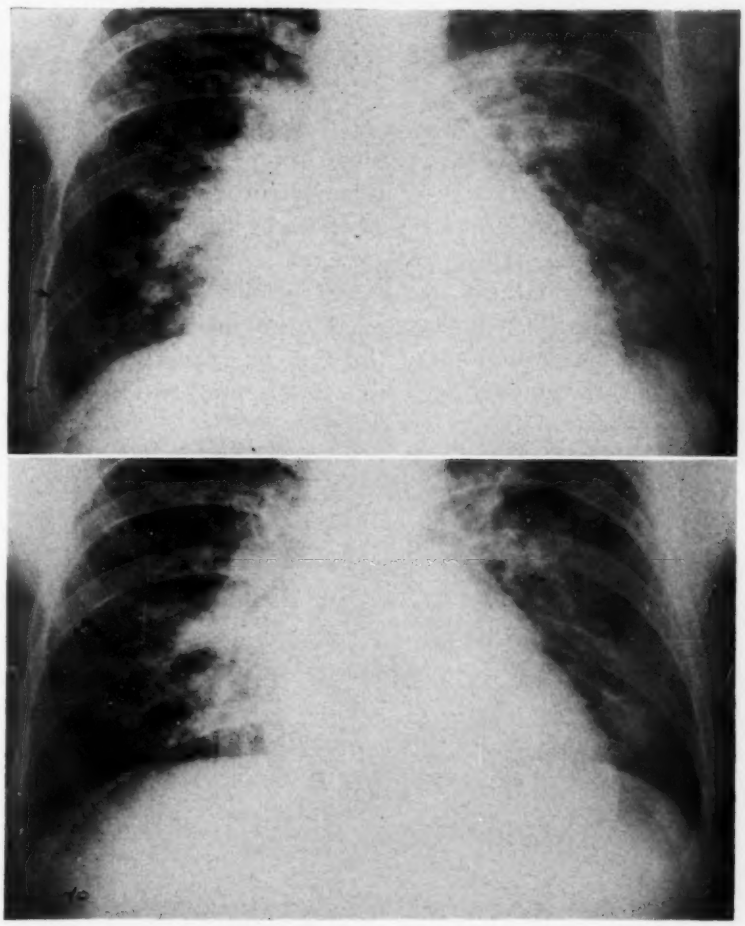
but as the veins increase in size they are usually surrounded by a network of lymphatics. The lymphatics accompanying the venous radicles which drain the bronchial tree also communicate with the bronchial lymphatics. However, most of the lymphatics which accompany the venous radicles arising from the pleura join the pleural lymphatic plexuses.

Fig. 2A.—N. Mc., 28-year-old male with chronic glomerulonephritis, severe systemic arterial hypertension, and repeated bouts of left ventricular failure.

Of special interest are the lymphatics of the interlobular septa. Miller[7] has demonstrated them to be intimately associated with the pulmonary veins. A rich network of lymphatics extends from the plexus which surrounds the veins into the septa, forming a cordon around the secondary lobules. A pleural plexus of lymphatics with free intercommunication is present. These interlobular lymphatics extend outward and join the pleural plexus of lymphatics at right angles. It is these interlobular lymphatics which, when dilated, cast their shadows on the roentgenograms and are manifested as the basal horizontal striations described previously. Miller notes that in lungs of animals which have a thick pleura with well marked connective tissue septa the interlobular structures are readily identifiable, whereas in those animals which have thin pleura, with no connective tissue septa, these structures are absent. A thin pleura is present in the cat, dog, rabbit, and rat, and a thick pleura in the ox, sheep, pig, and man. Individual differences of pleural thickness within the species might explain the absence of the roentgenographic finding under discussion in some persons with pulmonary hypertension and its presence in others. However, detailed studies of individual variations in pleural and interlobar septal thickness are not available.

While the transverse striae seen in the lung bases may thus represent the interlobular lymphatics which run at right angles to the pleural lymphatics, the so-called "slight pleural thickening" often noted along the lateral chest wall just above the costophrenic angles could well be the dilated lymphatics of the pleural plexus itself. The latter is often connected with the transverse striae, appearing roentgenographically in much the same manner as does minimal effusion in the horizontal interlobar pleural fissure extending into the major pleural space (Fig. 2).

B.



C.

Fig. 2.—*B* and *C*. N. Mc. same as Fig. 2*A*. *B*, Jan. 3, 1953. At this time the patient had marked pulmonary edema. The basal striae are prominent (arrows) as is the pulmonary alveolar edema. Along the lateral aspect of the right lung base there is a band of "pleural thickening" (lower arrow) which probably represents dilatation of lymphatics of the pleural plexus. The transverse striae represent the interlobular lymphatics. *C*, Jan. 7, 1953. The patient was considerably improved following medical treatment. The pulmonary alveolar edema has improved, and the lymphatic dilatation is no longer evident.

DIFFERENTIAL DIAGNOSIS

The roentgen appearance of pleural lymphatic dilatation is highly characteristic. When this finding was first encountered and before its significance became apparent it was thought to represent basal pulmonary emphysema. However, the markings due to dilated lymphatics are horizontal and parallel to each other; they do not have the arclike contours which extend in various directions as do the curvilinear shadows of pulmonary cysts, bullae, or obstructive emphysema. Furthermore, inspiration and expiration film pairs show that the characteristic pattern becomes less prominent and, in some cases, almost disappears on expiration films; the contrary usually occurs in pulmonary emphysema.

The lymphectatic markings also differ markedly from the "discoid" or "plate-like" atelectasis of Fleischner. Fleischner's lines generally appear singly though on occasion there may be two or three present. However, they never appear in as large numbers as do the basal striae of lymphatic dilatation and rarely assume the parallel transverse arrangement. Furthermore, Fleischner's lines do not originate in the periphery of the lung field to extend to the pleural surface.

Pulmonary arterial dilatation, venous congestion, and peribronchial thickening can all be readily differentiated from the lymphectatic markings under discussion since the latter show none of the typical vascular or bronchial arborization. Nor do they diminish in caliber as they extend peripherally.

TABLE I. DATA ON 24 CASES OF MITRAL STENOSIS WITHOUT BASAL PULMONARY STRIAE

CASE NO.	MEAN PUL. ART. PRESS. (MM. HG)		MEAN WEDGE PRESS. (MM. HG)	
	PREOPERATIVE	POSTOPERATIVE	PREOPERATIVE	POSTOPERATIVE
1.	21		13	
2.	22			
3.	46	38	38	
4.	30			
5.	85	59		22
6.	33	42		
7.	66	25	32	11
8.	91			
9.	49		29	
10.	43	26	21	
11.	26			
12.	48			
13.	38		21	
14.	29		19	
15.	19			
16.	31		18	
17.	79		37	
18.	42		21	
19.	28		15	
20.	65	39		
21.	22			12
22.	23			
23.	18			
24.	15			

Average mean pulmonary artery pressure (preoperative): 40 mm. Hg
Average mean wedge pressure (preoperative, 11 cases): 23 mm. Hg

MATERIAL

Chest roentgenograms of sixty-three patients with the clinical diagnosis of mitral stenosis were examined.* Each patient had been studied by right-heart catheterization; the pulmonary artery pressure was measured in all cases, the pulmonary wedge pressure in twenty-seven. Thirty-nine cases demonstrated the typical transverse basal striae. This was recorded as moderate or marked.

The significant data on these cases are tabulated in Tables I and II.

TABLE II. DATA ON 39 CASES OF MITRAL STENOSIS WITH BASAL PULMONARY STRIAE

CASE NO.	MEAN PUL. ART. PRESS. (MM. HG)		MEAN WEDGE PRESS. (MM. HG)		BASAL STRIAE	POST-OPERATIVE STRIAE
	PRE-OPERATIVE	POST-OPERATIVE	PRE-OPERATIVE	POST-OPERATIVE		
25.	52	27			Marked	D
26.	92	49	65(?)	10	Marked	A
27.	76	59			Marked	NC
28.	65	39	34		Marked	D
29.	97				Marked	A
30.	45		32		Marked	A
31.	85				Marked	A
32.	84				Marked	D
33.	57		28		Marked	A
34.	31				Marked	U
35.	43				Marked	NC
36.	65		29		Marked	U
37.	36				Moderate	A
38.	62	43			Moderate	I
39.	28	17			Moderate	NC
40.	12	17			Moderate	A
41.	50	38		13	Moderate	D
42.	36	30			Moderate	NC
43.	23	22	38	13	Moderate	D
44.	52	22	16		Moderate	A
45.	37	30			Moderate	A
46.	49		22		Moderate	A
47.	54				Moderate	U
48.	39	46			Moderate	NC
49.	30	19			Moderate	U
50.	48		32		Moderate	U
51.	47		27		Moderate	U
52.	30		14		Moderate	NC
53.	89		33		Moderate	NC
54.	97				Moderate	A
55.	47				Moderate	NC
56.	40				Moderate	U
57.	43				Moderate	A
58.	40				Moderate	A
59.	51		29		Moderate	U
60.	31		18		Moderate	A
61.	25		12		Moderate	D
62.	39				Moderate	A
63.	30				Moderate	U

Average mean pulmonary artery pressure (mm. Hg):
Entire group (39 cases): 50
Marked striations (12 cases): 66
Moderate striations (27 cases): 43

Average mean pulmonary wedge pressure (mm. Hg):
Entire group (15 cases): 29
Marked striations (5 cases): 38
Moderate striations (10 cases): 24

A = Absent
D = Decreased but still evident
NC = No change
U = No satisfactory follow-up study
I = Increased

*Many of these cases are included in a report by Richards and associates.[7]

The average mean pulmonary artery pressure of the twenty-four cases without striae was 40 mm. Hg; it was 50 mm. Hg in the thirty-nine cases with striae. Twenty-seven cases showed moderate basal streaking and their average mean pulmonary artery pressure was 43 mm. Hg. Twelve cases showed marked basal striae, and the average mean pulmonary artery pressure of this group was 66 mm. Hg.

The pulmonary wedge pressure was known in twenty-six cases. Eleven showed no basal striae; the average mean wedge pressure of this group was 23 mm. Hg. Ten cases showed moderate basal striae; their average mean wedge pressure was 24 mm. Hg. The five cases showing marked basal streaking had an average mean wedge pressure of 38 mm. Hg.

The patients without basal striae varied in age from 11 to 55 years and those with striae from 17 to 60 years.

No relationship could be established between the lymphectasia and the duration of the disease, as judged from the known onset of symptoms or preceding attacks of rheumatic fever. There was no significant difference in the occurrence of hemoptysis, orthopnea, or pulmonary edema in those with and in those without the basal striae.

It is evident, then, that positive correlation existed between the degree of basal pulmonary striae and the pulmonary arterial and wedge pressures. These pressures were significantly higher in the group of patients with basal striae than in those without striae. Those with marked striae had higher pressures than those with only moderate striae. While many patients with severe pulmonary arterial hypertension failed to show evidence of interlobular lymphatic dilatation, only one patient with basal striations (present to minimal degree) had a mean pulmonary artery pressure of less than 20 mm. Hg. The pulmonary wedge pressure was not obtained in this case.

At no time has pulmonary basal striation been seen in otherwise normal chest roentgenograms.

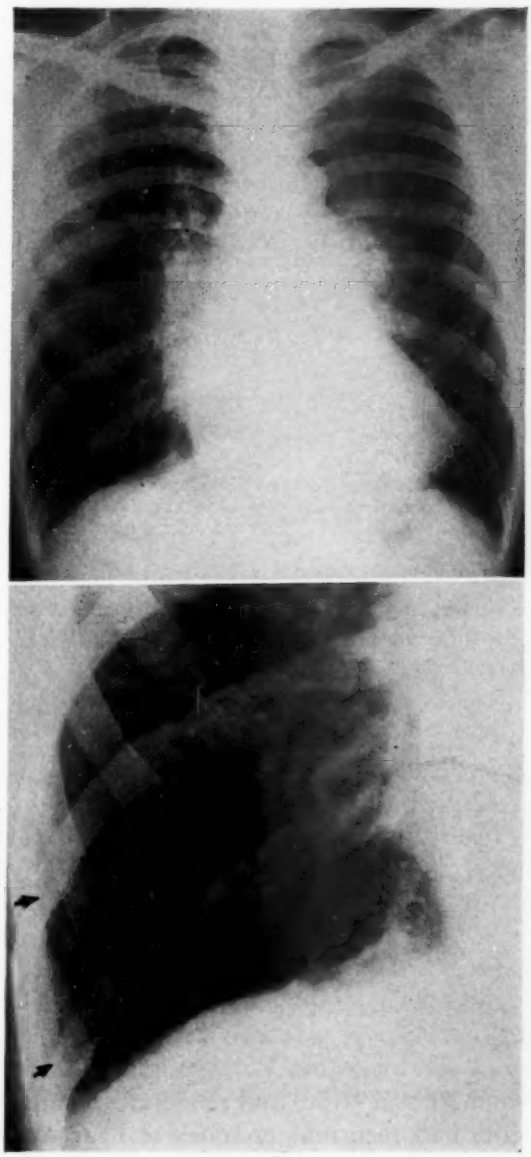
Considering it unlikely that such a pattern of pulmonary markings would reflect a specific etiologic entity, such as mitral stenosis, it was thought that it could reflect pulmonary hypertension, thus having physiologic rather than a purely etiologic significance. The previously noted correlation would favor this possibility. With this in mind, twenty cases of congenital heart disease with marked pulmonary hypertension were reviewed. The average pulmonary artery pressure of this group was 105/55 mm. Hg. In this group there was no case with dilated pleural lymphatics. Thus, there was no positive correlation between the presence of basal pulmonary striae and pulmonary hypertension of other than mitral stenosis etiology.

To determine whether there is any correlation between lymphatic dilatation and increased blood flow through the pulmonary circuit fifty cases of congenital heart disease in persons over 10 years old, chosen consecutively from the files, were studied. This group included patent ductus arteriosus, interventricular and interatrial septal defects, and a few acyanotic cases in which the diagnosis was in doubt. Most had had right-heart catheterization. The pulmonary artery pressures varied from normal to markedly elevated. In no case was

there clinical evidence of left ventricular failure. No basal pulmonary striae were present in any case.

The chest roentgenograms of twenty-three men with left ventricular failure were then studied. This group has been reported on previously by Borden and associates.[9] The etiology of the heart disease was systemic arterial hypertension in eleven patients, syphilitic aortic insufficiency in two, rheumatic aortic insufficiency in five, aortic stenosis in one, and aortic stenosis and insufficiency

A.



B.

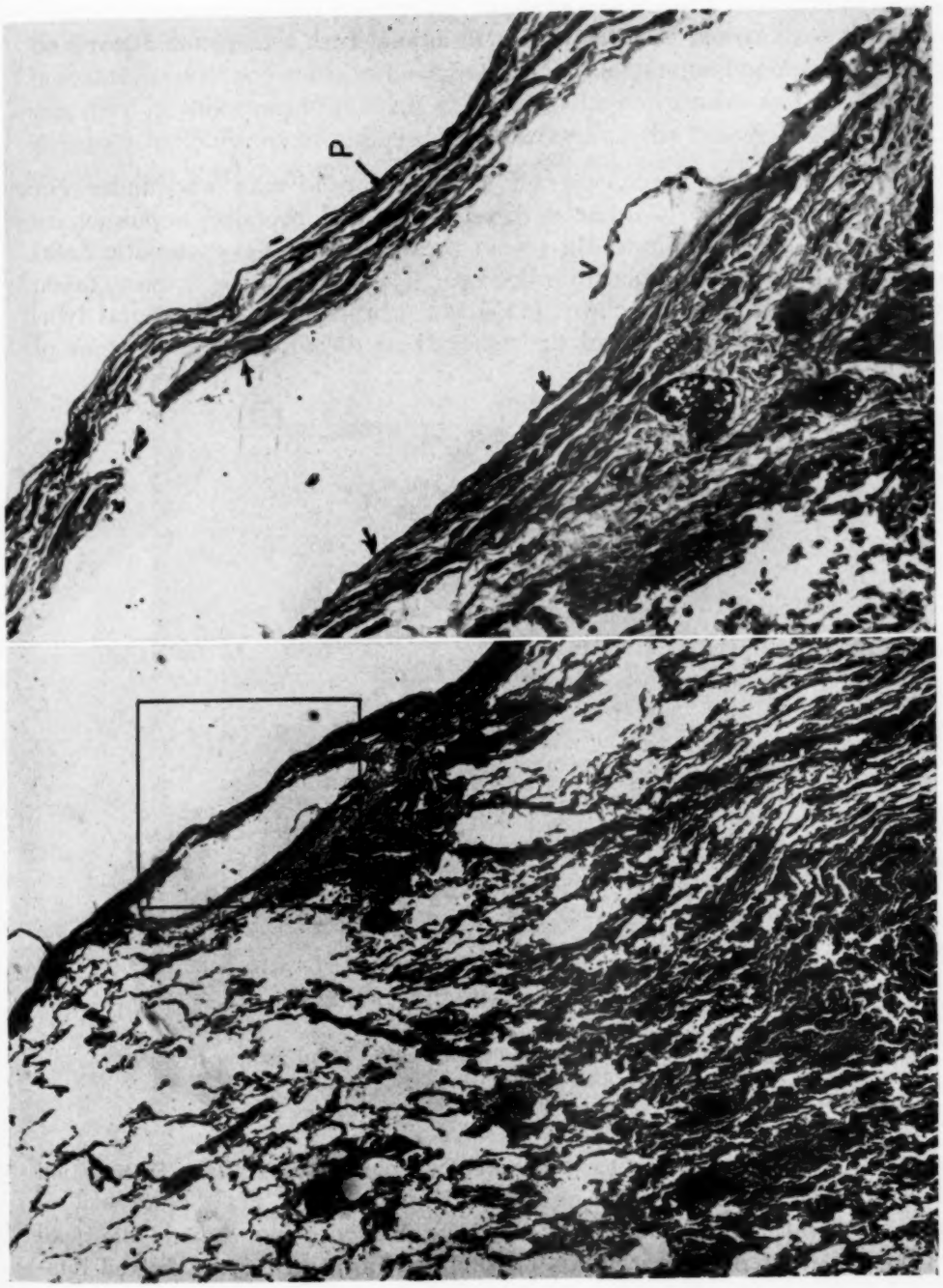
Fig. 3.—GH., 46-year-old male with mitral stenosis. *A*, Mean pulmonary artery pressure, 65 mm. Hg. *B*, Pleural lymphatic dilatation is present in both bases (arrows), somewhat more so on the right.

in four. Some increase in the pulmonary artery pressure was present in all but three patients, the average pressure for the group being 38/18 mm. Hg. No case showed any evidence of basal striae. Chest films of an estimated 300 patients seen at the University Hospitals and outpatient clinics because of arteriosclerotic or hypertensive heart disease, many in frank failure, were reviewed. Only two cases showed basal striae, both minimal. One was a 57-year-old man with hypertensive cardiovascular disease and repeated episodes of left-sided failure, and the second was a 69-year-old male with arteriosclerotic heart disease and one episode of coronary occlusion.

Fig. 4.—Same patient as Fig. 3. Gross specimen of biopsy of left lower lobe obtained at time of mitral commissurotomy. *A*, Dilated pleural lymphatics. *B*, Hemostat jaws.

Further study uncovered a case with dilated pleural lymphatics in a patient suffering from coarctation of the aorta. The pulmonary artery pressure was 85/40 mm. Hg. This man had had repeated bouts of left ventricular failure. The lymphectasia in this case was obviously related to the heart failure rather than to the congenital cardiovascular disease.

In the course of this study the possibility that the basal striations were due to interlobular septal edema was considered. Thus, the chest films of thirty patients with severe hypoproteinemia were chosen at random and studied. This group included twelve patients with chronic glomerulonephritis, eight with ulcerative colitis, and ten with atrophic hepatic cirrhosis. One patient had very prominent basal pulmonary striations as well as marked alveolar edema (Fig. 2). This patient suffered from severe chronic glomerulonephritis and systemic arterial hypertension (190/110 mm. Hg). As the alveolar edema improved with treatment the basal striae became less prominent. The only other patient of this group to show basal striae was also a case of chronic glomerulonephritis with systemic arterial hypertension of 170/100 mm. Hg. The only film on this patient revealed minimal basal striae and moderate pulmonary alveolar edema. Both of these patients had recurrent episodes of heart failure and pulmonary edema. Five patients in this group of thirty showed alveolar edema but no basal striae; four suffered from chronic glomerulonephritis and one from atrophic hepatic cirrhosis.



A. *B.*

Fig. 5.—Photomicrographs of specimen shown in Fig. 4. (*A*, × 20; *B*, × 80; reduced ¼.) *P*, Pulmonary pleural surface. *V*, Lymphatic valve. Arrows, Endothelial cells lining the dilated lymphatics.

The chest roentgenograms of eight dogs with experimentally produced mitral stenosis and pulmonary hypertension were examined. Contrary to expectations no basal lymphatic dilatation was evident. However, this became understandable when it was learned that the dog is an animal with thin pleura, having no interlobular septa or lymphatics.

PATHOLOGY

Fig. 3 is the chest roentgenogram of a 46-year-old man who underwent mitral commissurotomy. Cardiac catheterization had revealed a pulmonary artery pressure of 108/48 mm. Hg (mean pressure, 65). Characteristic basal striations are present to a moderate degree. The gross lung specimen, taken from the left lower lobe, is shown in Fig. 4. Markedly dilated pleural lymphatics were grossly evident, and the removed portion of lung showed one of

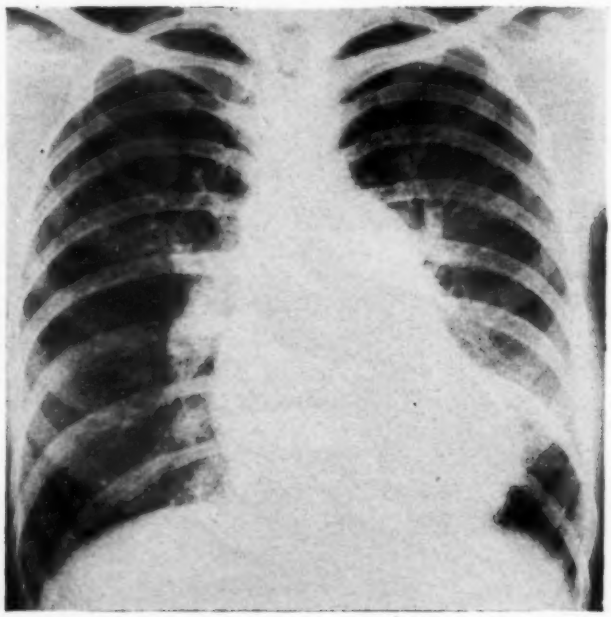


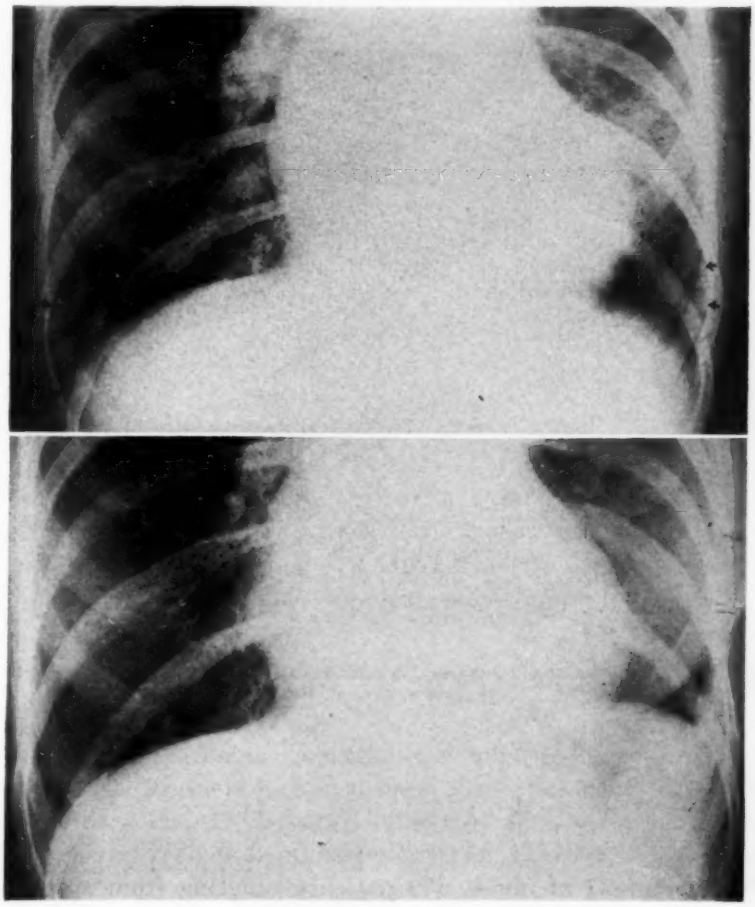
Fig. 6A.—D. J., 27-year-old female with mitral stenosis. Mean pulmonary artery pressure, 84 mm. Hg.

the dilated branching lymphatics. The microscopic specimen (Fig. 5) revealed marked pulmonary passive congestion. Pigment-loaded macrophages were present. Several dilated endothelial-lined vessels with no appreciable wall could be seen located subpleurally. These vessels appeared to be dilated lymphatics.* The sections failed to reveal interlobular lymphatic dilatation, probably because the sections were so oriented as not to show this feature best.

*Dr. Jesse E. Edwards was kind enough to review the sections and agreed that these vessels were definitely dilated lymphatics.

Biopsies have generally been disappointing. The sections frequently show dilated pleural or subpleural spaces. These have, for the most part, been considered local areas of emphysema or sectioning artifacts. Close re-examination, however, has revealed endothelial lining in some of these spaces. It would probably be well to fix the removed sections of lung with the clamps left on, as was done in this case, to prevent collapse of the lymphatics and facilitate their identification. It would also be useful to section the biopsy specimens in the proper plane in relation to the interlobular lymphatics.

B.



C.

Fig. 6.—*B* and *C*. Same case as Fig. 6*A*. *B*, Dec. 29, 1952. The dilated pleural lymphatics are evident in both bases (arrows). *C*, Feb. 4, 1953. A successful mitral commissurotomy was performed on Jan. 8, 1953. The basal striae are now barely discernible.

PHYSIOLOGIC CONSIDERATIONS

We must turn to the study of pulmonary hemodynamics for the answer to the question of why dilated interlobular and pleural lymphatics are confined almost entirely to persons with pulmonary hypertension secondary to mitral stenosis.

This probably is a reflection of sustained elevated left atrial pressure with consequent pulmonary venous and capillary hypertension. The mechanism is probably similar to that found in the systemic circulation in dogs with experimental inferior vena cava constriction. Hoffbauer and associates[10] found that in such animals, as the portal vein pressure rose, the lymphatic channels draining the liver were enormously dilated and tortuous, indicating a greatly increased lymph flow from the liver. White and co-workers[11] proved in an experiment with an unanesthetized dog that increase in venous pressure caused a prompt rise in lymph flow. With elevated pulmonary venous and capillary pressures the lymphatics may well serve as a device to carry away the transudate which

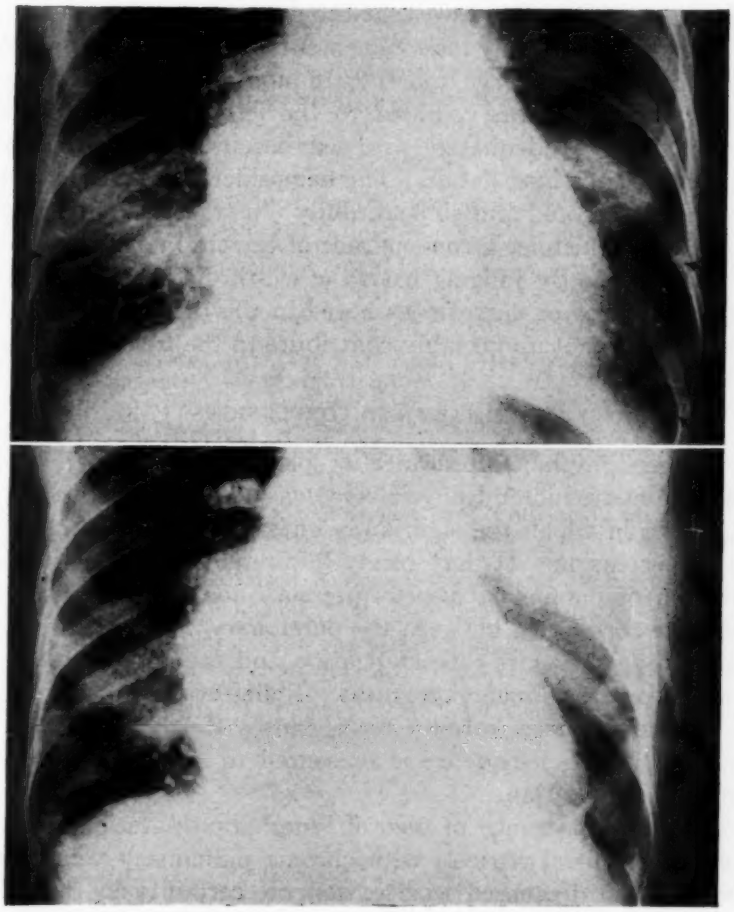
Fig. 7A.—C. P., 39-year-old female with mitral stenosis. Mean pulmonary artery pressure, 43 mm. Hg.

may have otherwise caused pulmonary alveolar edema. This may explain why such edema is not more frequently seen in mitral stenosis, especially when the pulmonary venous pressure is markedly elevated. In no other disease is left atrial pressure so likely to be chronically sustained at high levels. It should be recalled that in only 2 of about 300 patients suffering from systemic arterial hypertension or arteriosclerotic heart disease, many with repeated episodes of left ventricular failure, was pleural lymphatic dilatation evident. In such cases the left ventricular failure is usually intermittent; the chronic elevation of pulmonary venous and capillary pressures due to mechanical obstruction, as is present in mitral stenosis, is lacking. Occasionally, left ventricular failure may be chronic with chronic elevation of pulmonary venous and capillary pressures. Under this circumstance lymphatic dilatation can probably occur.

As would be suspected, if the mechanism of lymphatic dilatation is as noted previously, the cases of septal defect and patent ductus arteriosus failed to show

basal striae even though the shunt was as much as four to eight times the systemic flow. In such cases the pulmonary arterial pressure is generally normal or only moderately elevated, this probably being due to pulmonary arteriolar sclerosis. These patients do not have increased pulmonary venous pressure unless failure develops. Swan and his associates[12] reported no elevation of the pulmonary arterial "wedge" pressure in any of their cases of patent ductus arteriosus, interventricular defect, and interatrial defect.

B.



C.

Fig. 7.—*B* and *C*. Same case as Fig. 7A. *B*, March 10, 1952. Marked pleural lymphatic dilatation is present in both bases (arrows). *C*, July 6, 1953. Mitral valvulotomy was performed on June 2, 1953. Basal striae are still present though less prominent than in the preoperative study.

The two patients with chronic glomerulonephritis had left-heart failure which persisted over an extended period of time. This could account for elevated pulmonary venous and capillary pressures and hence increased lymph flow.

From the foregoing considerations one would expect clearing of the basal striae following lowering of the pulmonary venous pressure by mitral commis-

surotomy. As noted in Table II this frequently proved to be true. In many cases with satisfactory postoperative roentgenograms there was definite improvement; in some the roentgenographically evident lymphectasia disappeared completely (Figs. 6 and 7). In their report Fleischner and Reiner[5] noted the disappearance of the basal striae in a case of mitral stenosis following successful valvuloplasty. The failure of complete disappearance of the lymphatic striae in all cases with surgical relief of mitral stenosis and pulmonary hypertension can perhaps be attributed to the chronic lymphatic engorgement with consequent thickening of the walls of the lymphatics, sufficient to cast a shadow on the film. Also, it is well known that the dynamic changes in the pulmonary artery and wedge pressures may take some months to occur and anatomic changes, i.e., reduction in heart size, may take 6 to 18 months. In a few instances where the lymphatic dilatation was confined to the left base the postoperative appearance could not be adequately assessed because pleural effusion or fibrin deposition obscured the lung detail. The hemosiderin deposition which Fleischner and Reiner have noted and so beautifully illustrated in their report is probably no more than a histologic concomitant of the chronic heart disease and the lymphatic dilatation. By judging from the width of the basal striae and their frequent disappearance or decrease as noted in the present study it is felt that the hemosiderin does not appreciably contribute to the basal shadows as seen on the roentgenogram.

SUMMARY AND CONCLUSIONS

The roentgenographic appearance of pleural lymphatic dilatation is described, and the anatomic and physiologic considerations discussed. The great majority of cases in which the sign is present are cases of mitral stenosis with pulmonary hypertension. It may rarely be present in cases with chronic sustained elevation of pulmonary venous pressure due to left ventricular failure. There is positive correlation between the pulmonary artery and wedge pressures as determined by right-heart catherterization and the degree of lymphatic dilatation as noted on chest roentgenograms. Relief of pulmonary venous hypertension by mitral commissurotomy often causes the lymphectasia to decrease or disappear. Histologic evidence is presented to prove the presence of the pleural lymphatic dilatation.

The roentgen appearance of pleural lymphatic dilatation is characteristic. When it is noted, mitral stenosis with chronic pulmonary venous and arterial hypertension can be diagnosed with reasonable certainty in the vast majority of instances.

SUMMARIO E CONCLUSIONES IN INTERLINGUA

Es describite le configuration roentgenographic de dilatate vasos lymphatic pleural. Le phenomeno es discutite ab le puncto de vista anatomic e physiologic. Le grande majoritate del casos con iste signo es casos de stenosis mitral con hypertension pulmonar. In rar casos le signo pote presentar se in patientes con continue elevation chronic del pression venose pulmonar debite a insufficientia sinistroventricular. Il existe un correlation positive inter (1) le pression del arteria pulmonar e cuneate pressiones (determinate per catheterisation dex-

terocardiac) e (2) le grado de dilatation lymphatic notate in le roentgenogramma thoracic. In multe casos le allevation del hypertension pulmonovenose per commissurotomia mitral resulta in un reduction o le disparition del lymphectasia.

Le configuration roentgenographic de dilatate vasos lymphatic pleural es characteristic. Quando iste configuration es constatate, le diagnose de stenosis mitral con chronic hypertension pulmonar venose e arterial es satis certe in le vaste majoritate del casos.

The author is deeply indebted to many members of the staff of the Variety Club Heart Hospital, University of Minnesota, for the aid and encouragement which made this study possible. I am especially grateful to Dr. Craig W. Borden for making available the cardiac catheterization data and for invaluable advice concerning cardiopulmonary physiology, and to Dr. Ivan D. Baronofsky, who performed all the mitral commissurotomies in this series, for the biopsy material, the dog chest roentgenograms, and stimulating discussions, and encouragement.

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ELEVATED RIGHT VENTRICULAR PRESSURE

Its Relation to the Pattern of Right Ventricular Hypertrophy

M. Torner-Soler, M.D., I. Balaguer-Vintró, M.D., and
J. Gibert-Queraltó, M.D.

Barcelona, Spain

THE frequent use of cardiac catheterization in the study of many congenital and acquired heart diseases has permitted correlating the hemodynamic data with the electrocardiographic (ECG) pattern. Lenègre and co-workers[1] established a relation between the main right ventricular pressure and the ECG pattern, finding that in diseases with elevated right ventricular pressure the ECG showed alteration of the R/S ratio in Lead V_1 or in Leads V_1 and V_6 and a deviation of the QRS-axis toward the right. Johnson and co-workers[2] studied forty cases of cor pulmonale, observing a relation between the arterial pulmonary pressure and the ECG pattern of right ventricular hypertrophy. Gordon and Goldberg[3] studied this relation between hemodynamics and ECG pattern in twenty-one cases of congenital heart disease. Later on, Cosby and co-workers[4,5] studied these relations in patients with congenital heart disease and with mitral stenosis, settling differences between both groups. Schweizer and co-workers[6] compared the hemodynamics and ECG data with the autopsy findings in twenty-nine cases, deducing that the existence of a left ventricular hypertrophy may mask the ECG signs of right ventricular hypertrophy and observing a greater intensity of the ECG alterations in mitral stenosis than in cor pulmonale.

MATERIAL AND METHOD

Hemodynamic data have been compared with ECG pattern in fifty cases distributed in the following way: congenital heart disease, twenty-five cases; mitral stenosis, fourteen cases; cor pulmonale, five cases; multiple valvular disease, in which mitral stenosis predominated, six cases.

All of these cases have been studied clinicoradiologically and electrocardiographically. Under the hemodynamic data, besides the study of pulmonary artery and ventricular pressure, most of them have data as to pulmonary or right ventricular flows.

From the ECG point of view, special attention was given to the following aspects: form of the ventriculogram, QRS-axis, activation time Lead V_1 and height of R in Lead V_1. All these data have been related to the degree of right ventricular hypertension and the volume of pulmonary or right ventricular flows.

From the School of Cardio-Angiology of the University of Barcelona, Spain; Director: Prof. J. Gibert-Queraltó, M.D.

Received for publication Oct. 29, 1954.

RESULTS

Relation Between the Right Ventricular Hypertension and the Ventriculogram Type.—In Fig. 1 we have distributed our cases according to the degree of right ventricular hypertension and the ECG pattern. We have observed four ventriculogram types: normal pattern, right bundle branch block, right ventricular hypertrophy, and a mixed pattern of hypertrophy and right bundle branch block, taking as such those right bundle branch block patterns with the second positivity of high voltage in Lead V_1 (Fig. 2).

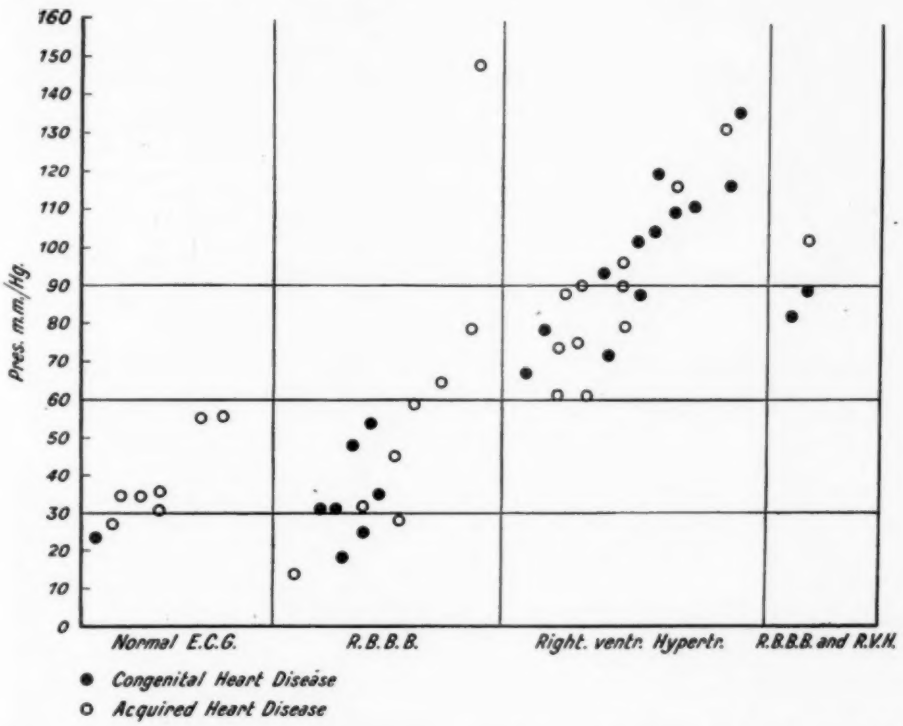

Fig. 1.—Elevated right ventricular pressure. Its relation with the patterns of normal electrocardiogram, right bundle branch block, right ventricular hypertrophy, and right bundle branch block and right ventricular hypertrophy.

Relating the different types we found a normal ECG with right ventricular hypertension in only one patient with congenital heart disease and seven with acquired heart diseases. The patient with congenital heart disease had a right ventricular systolic pressure below 30 mm. Hg, whereas among the patients with acquired heart disease there were cases with normal pressures and cases with hypertension, although in no case did it exceed 60 mm. Hg.

In the cases with complete or incomplete right bundle branch block we observed that they can be present at all pressure levels, although only in very special cases are they observed with a higher pressure than 90 mm. Hg.

The hypertrophy pattern which we have always considered as an inversion of the R/S ratio with delay of activation time in Lead V_1 has not appeared in any case with right ventricular systolic pressure lower than 60 mm. Hg, both

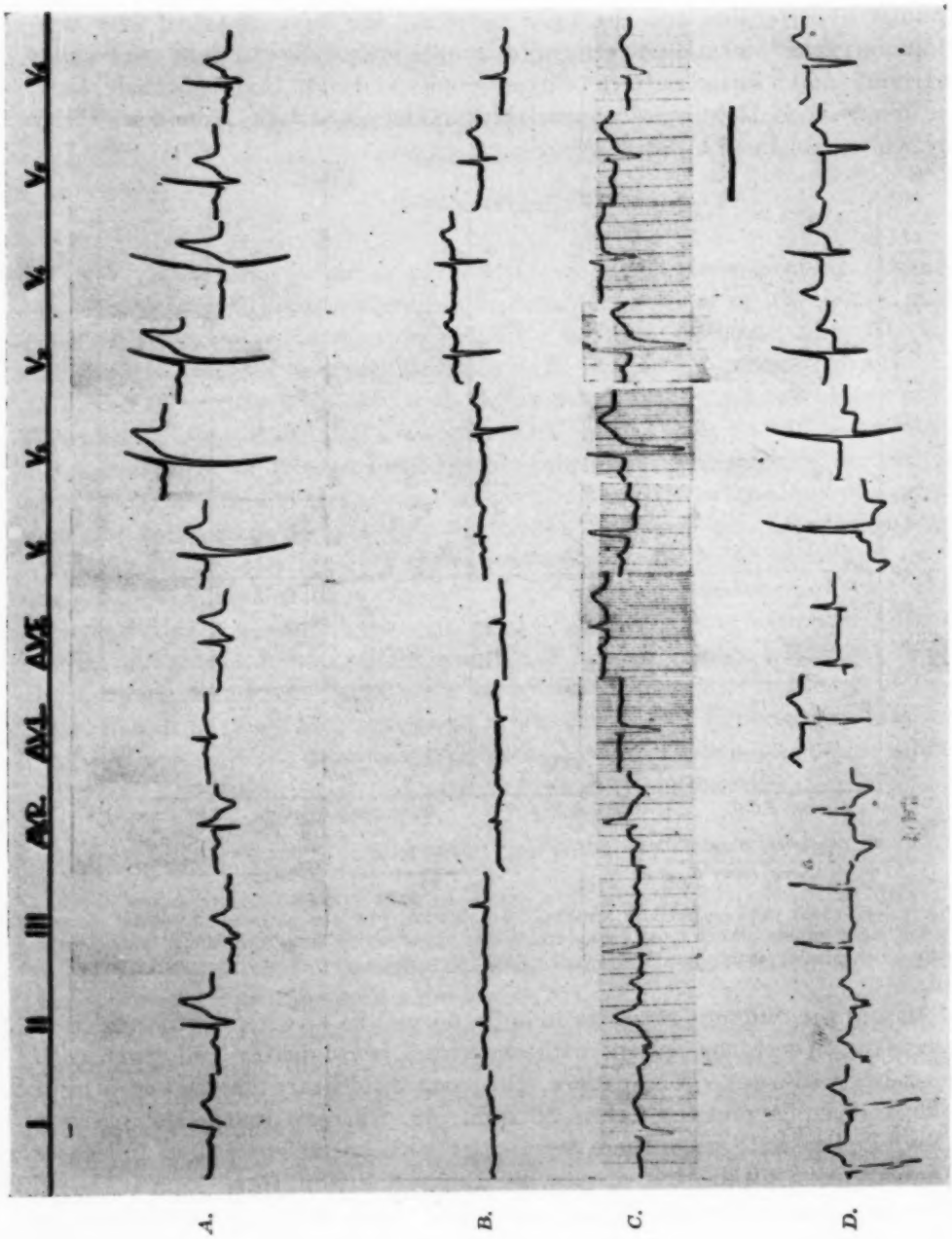

Fig. 2.—The four types of ventricular pattern. *A*, Normal pattern. *B*, Right bundle branch block; *C*, Right ventricular hypertrophy and *D*, mixed pattern of right ventricular hypertrophy and right bundle branch block.

in congenital and acquired heart disease. In three cases we have found the mixed pattern of hypertrophy and right bundle branch block, and in all there existed a marked right ventricular hypertension. In two of them the flow through the right ventricle was high. In one because there existed a complete drainage of pulmonary veins into the right auricle (autopsy) and in the other because of cor pulmonale, which suggested that the diastolic overcharge of the right ventricle takes part in the blocking genesis.

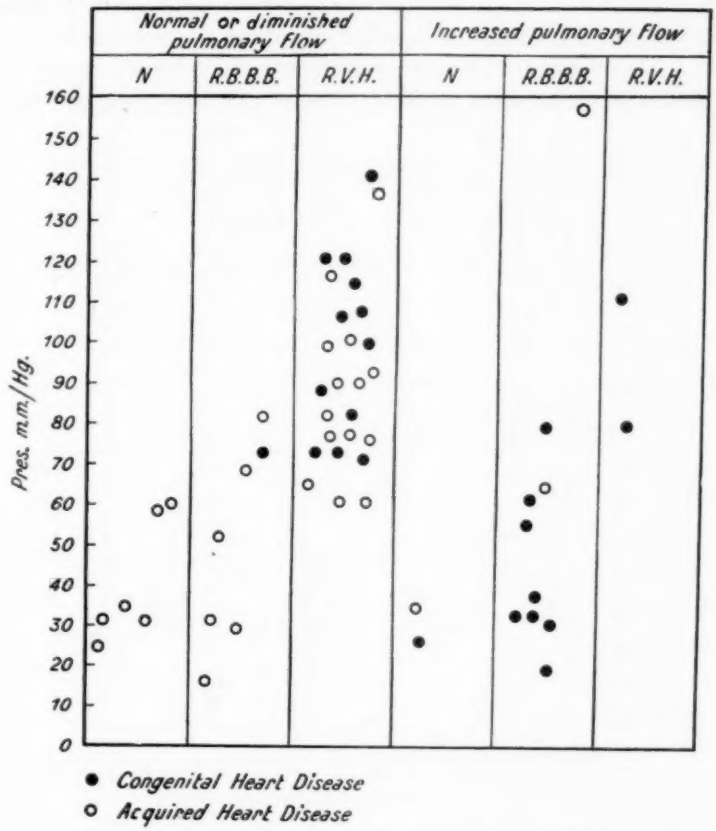

Fig. 3.—Relations between right ventricular pressure, the type of ventricular pattern and the value of pulmonary flow.

Relation Between the Ventricular Pattern Type, the Right Ventricular Hypertension, and the Value of Pulmonary Flow.—In Fig. 3 we have distributed the cases according to right ventricular hypertension and the amount of pulmonary flow. It will be observed that only two with a normal pattern had an increased pulmonary flow. One of them had a ventricular septal defect with a normal pulmonary pressure and the other had a cor pulmonale with a slight pulmonary hypertension. The remaining cases had normal pulmonary flow.

The blocking pattern appeared in both groups, congenital as well as acquired, whereas all except one in the group with congenital heart disease had an increased pulmonary flow, all but two patients with acquired heart disease belong to the group with normal or diminished pulmonary flow. This superiority of the congenital heart disease in the group with increased pulmonary flow depends

on the large number of septal defects, especially interauricular, whose diastolic overcharge for the right ventricle is the cause of blocking. In the acquired heart disease the right bundle branch block genesis remained confused.

The cases with a right ventricular hypertrophy pattern appear in almost all of the group with normal or diminished pulmonary flow, in congenital as well as acquired heart disease, and all of them had right ventricular systolic pressure higher than 60 mm. Hg. Only in two cases appears right ventricular hypertrophy with increased flow. Both had congenital heart disease and in one the autopsy showed the existence of a total drainage of pulmonary veins into the right auricle. There was besides the right ventricular hypertrophy ECG pattern, the right bundle branch block pattern, which can be explained by its diastolic overcharge.

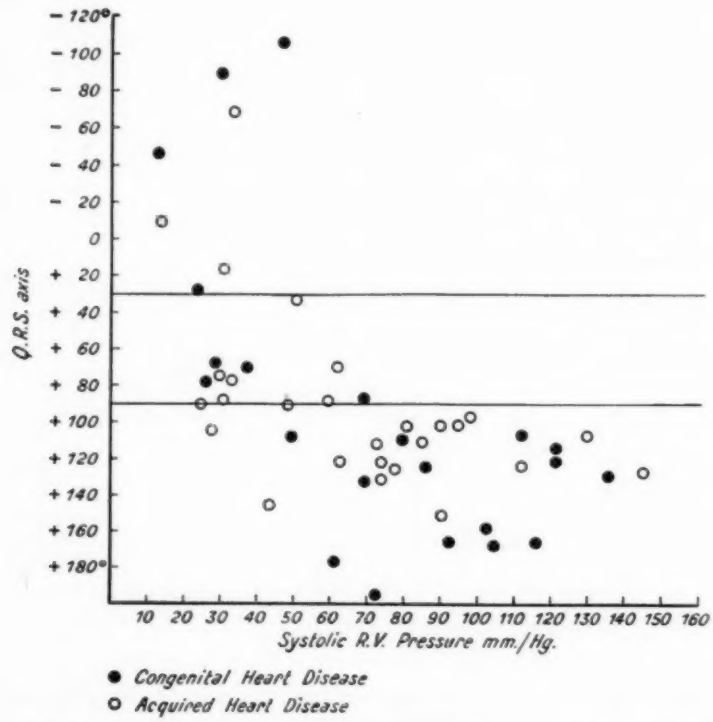

Fig. 4.—Relations between the right ventricular hypertension degree and the QRS-axis deviation.

Relation Between the Right Ventricular Hypertension Degree and the QRS-axis Deviation.—Fig. 4 demonstrates a clear relation between the degree of right ventricular hypertension and the deviation of the QRS-axis toward the right. In the figure, two horizontal lines appear; above the superior line the axis deviates toward the left and below the inferior line the axis deviates toward the right. Between the lines we find the normal axis, between 30 and 90 degrees. As one can see the normal axis or the ones deviated toward the left are always found among the cases with normal or slightly increased right ventricular pressure. No electric axis is normal, when the right ventricular systolic pressure exceeds the 70 mm. Hg in all but three cases where the QRS-axis deviation toward the right was higher than 90 degrees, the right ventricular systolic pressure was higher than 60 mm. Hg.

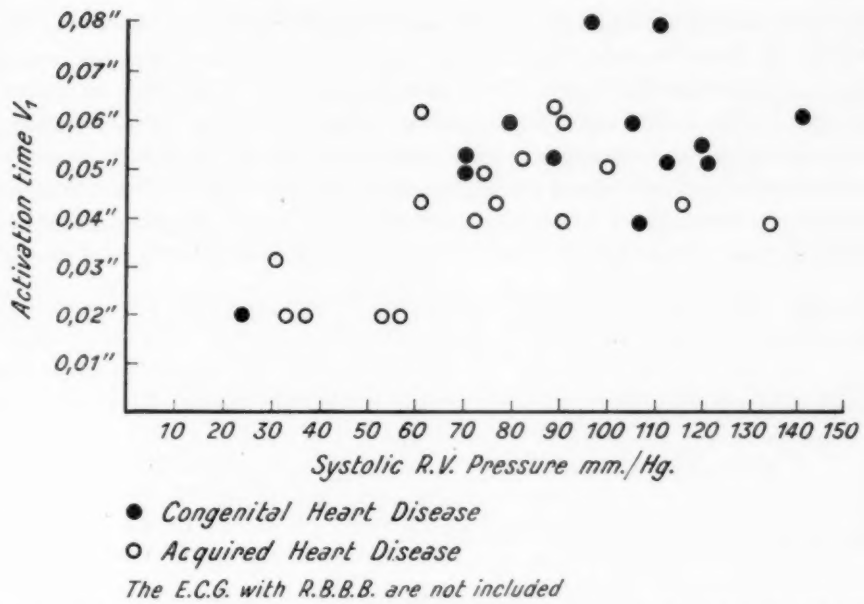

Fig. 5.—Relations between the right ventricular hypertension and the delay of activation time in V_1 lead.

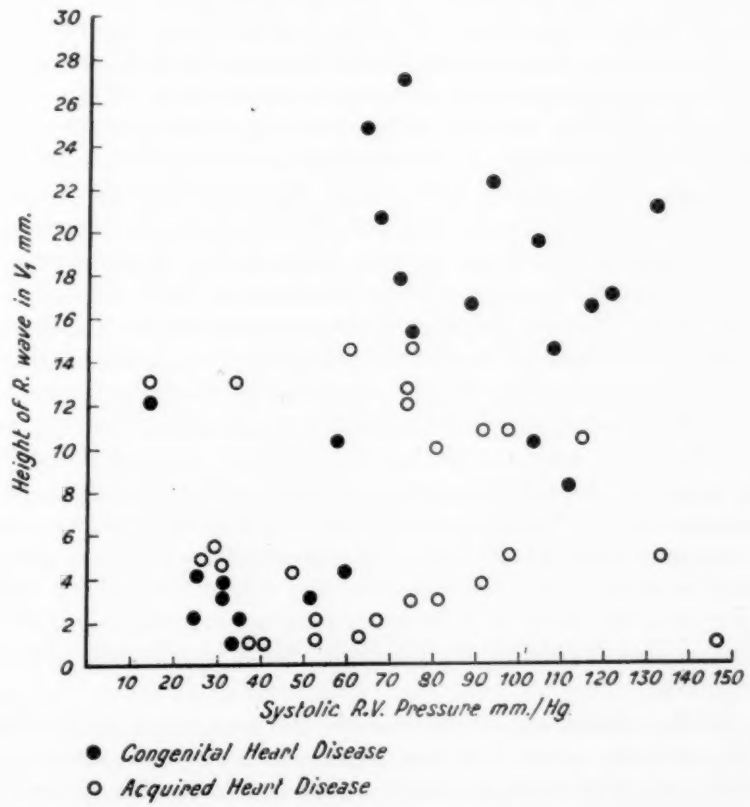

Fig. 6.—Relations between the height of R in V_1 lead and the right ventricular hypertension degree.

Relation Between the Right Ventricular Hypertension and the Delay of Activation Time in Lead V_1.—In Fig. 5 all the cases are included except the ones which presented a right bundle branch block pattern, in order to be able to relate more clearly the right ventricular hypertension with the delay of activation time. One can see that the ventricular activation time exceeds 0.04 sec. in cases with right ventricular systolic pressure higher than 60 mm. Hg. There is a remarkable difference between the patients with congenital and acquired heart disease, as with the same hypertension the activation time is more marked in the first.

Relation Between the Height of R in Lead V_1 and the Right Ventricular Hypertension Degree.—A study of Fig. 6 shows that in patients with congenital heart disease, the height of R in Lead V_1 increases with the degree of hypertension, which is well marked in right ventricular pressures, higher than 60 mm. Hg. This relation is, on the contrary, not observed in patients with acquired heart disease. Comparing the height of R in both groups, one observes that for the same degree of right ventricular hypertension, the height of R is much higher in patients with congenital heart disease.

DISCUSSION

Relating the ECG with the value of pressure and flow through the right ventricle, one observes a relation between the ECG pattern and the hemodynamic data, although there are evident differences if one compares congenital with the acquired heart disease. In congenital heart diseases the ECG is abnormal whenever the right ventricular systolic pressure is higher than 30 mm. Hg, or when there is an important flow increase through the right ventricle, that is, whenever the work of the right ventricle is increased, measured by the product of the flow and the pressure. The type of work which the right ventricle must perform is not the same if it is done on the basis of flow increase or of pressure. In the first the overcharge imposed on the right ventricle is a diastolic one, and in the second case it is a systolic overcharge. The type of ECG anomaly is different in both overcharge types. In the diastolic overcharge of the right ventricle, the observed ECG anomaly is a pattern of a complete or incomplete right bundle branch block, whereas in the systolic overcharge of the same ventricle the ECG shows the typical pattern of right ventricular hypertrophy characterized by the inversion of the R/S ratio and delay in activation time in Lead V_1. These differences in ventricular pattern and in relation with the overcharge type were already pointed out by Cabrera and Monroy[7] and agree exactly with our own results. In cases in which to the diastolic overcharge a marked right ventricular hypertension is added, we have observed the appearance of an ECG pattern to which we gave the name of a mixed hypertrophy pattern and blocking, and which we have seen appearing with a right ventricular systolic pressure higher than 60 mm. Hg.

Relating the ventricular pattern with the congenital heart disease type, we have seen that the normal pattern appears in those cases without ventricular hypertension and with little diastolic overcharge as in the ventricular septal defect type "Roger's disease". The right bundle branch block pattern appears

in most cases with auricular septal defect, whose diagnostic value we have already mentioned on other occasions.[8,9] In these cases a remarkable diastolic overcharge is combined with the normal or little increased right ventricular pressure. We have specially seen the right hypertrophy pattern in pulmonary stenosis, Fallot's trilogy and tetralogy; all these are accompanied by a marked systolic hypertension in the right ventricle, and among them the hypertrophy pattern has been most accentuated in cases of pulmonary stenosis with a closed ventricular septum, which are the ones that are accompanied by the greatest right ventricular hypertension. In some cases, the right ventricular hypertrophy pattern had a right blocking pattern added. In one case there was also found a diastolic overcharge of the right ventricle as mentioned previously.

In acquired heart disease, most with pure or predominating mitral stenosis, the ventricular pattern can remain normal in spite of the presence of pulmonary hypertension. We have seen that the hypertrophy pattern only appears with right ventricular pressures higher than 60 mm. Hg. In the paper by Cosby and co-workers[5] cases appear with the ventricular hypertrophy pattern, above as well as below this level, although in general the cases with normal or borderline pattern are situated below 60 mm. Hg. and the cases with hypertrophy pattern above this level. In acquired heart disease, in contrast to congenital heart disease, the right bundle branch block pattern appears always in relation to the increase of the diastolic overcharge of the right ventricle. The right bundle branch block appears as well in cases with increased as in diminished flows. The cases with increased flow belong to patients with cor pulmonale, in which the increased flow affects in the same way both ventricles, whereas in the cases with septal defects, the diastolic overcharge affects only the right ventricle, which makes it difficult to find a clear relationship between the block pattern and a diastolic overcharge, which affects equally both ventricular cavities.

Comparing the degree of axis deviation toward the right among the patients with congenital and the group with acquired heart disease, we realize that for the same degree of right ventricular hypertension the deviation of the axis toward the right is somewhat more accentuated in patients with congenital heart disease. These differences between both groups are still more accentuated on comparing the delay of activation time and the height of R wave in Lead V_1, which appear much more altered among the patients with congenital heart disease. These differences which agree with the results of Cosby and co-workers[5] could be explained because in congenital heart diseases the ventricular overcharge appears already at birth, as well as through the fact that the ventricular myocardium is allowed possibly to reach in these patients a higher degree of hypertrophy.

SUMMARY AND CONCLUSIONS

Among patients with heart disease, in whom a right-heart catheterization was performed, fifty cases with right ventricular hypertension have been chosen, in order to correlate the values of systolic pressure of the right ventricle with the ECG pattern. Besides in many of them the amount of pulmonary and right ventricular flow was determined; of these cases 50 per cent were patients with

congenital heart disease, and the other 50 per cent dealt with pure or predominating mitral stenosis and a certain limited number with cor pulmonale.

We have observed four types of ventriculogram: normal pattern, right bundle branch block, ventricular hypertrophy pattern, and a mixed pattern of hypertrophy and blocking. The latter pattern has served us to designate the tracings with right bundle branch block and high R wave in Lead V_1.

There are some differences in the relation of these patterns with the values of the systolic pressure of the right ventricle among the patients with congenital and acquired heart disease. There exists no normal pattern in patients with congenital heart disease with pressures over 30 mm. Hg. Above these values we find the ventricular hypertrophy pattern when the right ventricle suffers a systolic overcharge. The diastolic overcharge, that is to say, an increase in pulmonary flow with or without right ventricular hypertension, produces the right bundle branch block pattern. The blocking patterns and hypertrophy coincide in patients with marked right ventricular hypertension and increased flow through the right ventricle.

In acquired heart disease we usually find normal or borderline tracings, when there is no right ventricular hypertension or when this does not surpass 60 mm. Hg. Above this value right ventricular hypertrophy tracings appear. The right bundle branch block is found at all pressure levels, generally below 80 mm. Hg, but its genesis remains confused.

Whereas in congenital heart disease a clear relation was found between the right bundle branch block pattern and the increase of pulmonary flow, most cases of acquired heart disease with right bundle branch block had a normal or diminished pulmonary flow. There is an evident relation between the values of systolic hypertension of the right ventricle and the deviation of the QRS-axis. The normal axis or the ones deviated toward the left are always found in cases with normal or slightly elevated pressures. The QRS-axis is deviated toward the right in all the cases with right ventricular hypertension higher than 70 mm. Hg.

Relating the right ventricular hypertension with the activation time of the right ventricle measured in Lead V_1, one observes that in all cases with a higher pressure value than 60 mm. Hg, the ventricular activation time is longer than 0.04 sec., the delay in activation time being parallel to the degree of hypertension, (higher in congenital heart disease than in acquired).

In patients with congenital heart disease there exists a relation between the degree of right ventricular hypertension and the height of the R wave in Lead V_1. This relation is not very remarkable in the group with acquired heart disease, as in the latter the R wave is much less high for identical tension values. The greatest degree of alteration of activation time and height of the R wave in Lead V_1 in patients with congenital heart disease may be attributed to a greater ventricular hypertrophy due to a longer duration of the heart disease and the different conditions of the ventricular myocardium.

SUMMARIO IN INTERLINGUA

Esseva seligite, ab un serie de patientes subjicite a studios de catheterisation, cinquanta casos con elevate pression dextero-ventricular, con le objectivo de establir un correlation inter le valores de iste hypertension e le configuration del electrocardiogramma.

Nulle electrocardiogrammas normal esseva observate in casos congenite con pressiones supra 30 mm Hg. In casos de morbo acquirite, electrocardiogrammas normal occurreva con pressiones dexteroventricular de inter 30 e 60 mm Hg.

In casos congenite con pressiones infra 60 mm Hg, le anormalitate electrocardiographic esseva un configuration de bloco de branca dextere. In omne iste casos un augmentate fluxo de sanguine pulmonar esseva etiam constatate.

In casos de morbo acquirite, bloco de branca dextere es rar a omne nivellos del pression.

Usque pressiones de 60 mm Hg, le configuration de hypertrophia dexteroventricular esseva notate in ambe gruppos. Il existeva in iste casos un directe relation inter pression e configuration hypertrophic. Esseva constatate in plus un relation de (1) le altitude del unda R e le duration del activation in le derivation V_1 con (2) le nivello del pression dexteroventricular.

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THE ELECTROCARDIOGRAM IN MITRAL STENOSIS BEFORE AND AFTER COMMISSUROTOMY

J. GIBERT-QUERALTÓ, M.D., M. TORNER-SOLER, M.D., AND I. BALAGUER-VINTRÓ, M.D.

BARCELONA, SPAIN

IN another work[1] we analyzed the relation between the electrocardiographic (ECG) pattern and the value of systolic pulmonary and right ventricular pressure, observing that in mitral stenosis the right ventricular systolic pressure must be higher than 60 mm. Hg in order that an electrocardiographic pattern of right ventricular hypertrophy may appear. There exists a relation between the hypertension degree and the electrocardiographic pattern. This explains that in mitral stenosis not any signs of right ventricular hypertrophy appear until the pulmonary arterial hypertension reaches a certain level. When the hypertension is limited to the left auricle and pulmonary capillaries, the electrocardiographic alterations will be null or minimum. Therefore, the electrocardiographic modifications of right ventricular hypertrophy will be more evident when the gradient of tension between the arterioles and pulmonary capillaries is higher.

Besides the study of the different electrocardiographic types that the patients with mitral stenosis might present, one of the chief objectives of the present communication is the value of the study of the electrocardiographic modifications after commissurotomy, as it can be an exponent of the diminution of the pulmonary arteriolar resistances which will take place after the suppression of the valvular obstacle.

MATERIAL AND METHOD

We have studied sixteen cases of pure mitral stenosis. All these cases, besides the clinicoradiological record, have been studied hemodynamically by means of cardiac catheterization, and the following data have been obtained: pulmonary capillary pressure, pulmonary arterial and right ventricular pressure, cardiac output and cardiac index, total and arteriolar pulmonary resistance, mitral surface area after Gorlin's formula, diastolic mitral resistance index proposed by us, and the ratio between mitral resistance and arteriolar resistance (Table I). From these sixteen cases with electrocardiographic record before the commissurotomy, eight have been studied electrocardiographically up to one and one-half years after the operation.

From the School of Cardio-Angiology of the University of Barcelona, Spain; Director: Prof. J. Gibert-Queraltó, M.D.

Received for publication Oct. 29, 1954.

TABLE I. HEMODYNAMIC FINDINGS AT REST IN 16 CASES OF MITRAL STENOSIS

CASES	AGE	VASCULAR PRESSURES						CARDIAC OUTPUT		VASC. RESIS.		MITRAL AREA	MITRAL INDEX DIAST.	M.R. / P.A.R. QUOTIENT
		P.C.	P.A.P.			R.V.P.								
		M.	S.	M.	D.	S.	D.	L/M	L/M/M²	P.T.R.	P.A.R.			
1.	15	14	26	15	12	28	0	6	3.4	196	13	1.6	84	6.4
2.	21	14	36	17	10	29	0	5.3	3.6	255	45	1.5	130	2.9
3.	17	17	40	21	14	32	4	4	2.5	119	79	1.1	167	1.7
4.	19	19	40	24	16	60	0	4.4	2.8	438	98	1.1	354	3.6
5.	32	15	52	20	18	50	0	3.4	2.2	457	113	0.9	148	1.3
6.	36	33	96	63	40	98	0	5.8	3.4	869	434	0.9	291	0.6
7.	36	23	40	28	16	40	0	5.5	3.3	392	70	1.3	169	2.4
8.	32	—	—	—	—	90	0	3.4	2.4	—	—	0.9	—	—
9.	46	17	93	54	34	89	0	6	3.2	619	393	1	143	0.4
10.	8	19	86	74	60	85	0	3.2	2.8	1843	1369	0.7	272	0.2
11.	36	28	83	60	54	84	9	3.3	2.4	1451	679	1.3	506	0.7
12.	55	26	118	59	35	138	0	2.2	1.2	1240	693	0.4	501	0.7
13.	26	34	124	97	74	117	0	3.5	2.4	2315	1436	0.7	309	0.2
14.	25	13	39	28	20	38	0	6.4	4.2	337	187	2.1	79	0.5
15.	30	22	81	49	31	86	0	5.1	3.1	783	442	0.7	216	0.4
16.	34	27	59	41	32	56	0	3.7	2.5	869	291	0.8	354	0.8

P.T.R. = Pulmonary total resistance; P.A.R. = pulmonary arteriolar resistance.

TABLE II. ELECTROCARDIOGRAPHIC FINDINGS IN 16 CASES OF MITRAL STENOSIS

CASES	RHYTHM	QRS AXIS (DEGREES)	CLOCK-WISE ROTATION	LEAD V_1			T WAVE		P WAVE				
				PATTERN	ACT. TIME (SEC.)	R/S (SEC.)	V_1	DIII	AXIS	AMPL.	DUR. (SEC.)	MORPH.	VENTRICULAR PATTERN
1.	s	90	+	rS	0.03	0.3	—	—	n	1	0.08	n	N
2.	s	108	+++	rSR′	0.06	0.8	—	—	left	2.5	0.12	n	RBBB
3.	s	88	+	RS	0.03	0.5	—	—	left	2	0.12	mod.	N
4.	s	75	+++	rS	0.06	0.3	—	—	n	2	0.12	n	RVH
5.	s	10	+	rS	0.02	0.5	+	+	n	1	0.12	n	N
6.	s	120	+++	R	0.03	5	−	−	right	5	0.12	n	RVH
7.	s	74	+	RS	0.03	1.3	+	+	right	1.5	0.08	mod.	B
8.	s	105	+	Rs	0.04	8	+	+	n	0.5	0.08	n	RVH
9.	s	108	+++	qR	0.05	20	−	−	right	4	0.14	mod.	RVH
10.	s	130	+++	R	0.04	12	−	−	n	5	0.12	mod.	RVH
11.	a.f.	135	+++	R	0.06	8	−	−	——	——	——	——	RVH
12.	a.f.	110	+++	R	0.04	5	++	+	——	——	——	——	RVH
13.	s	126	+++	R	0.04	10	−	−	n	3	0.10	n	RVH
14.	a.f.	75	+	rsR′	0.08	0.5	−	−	——	——	——	——	R 3BB
15.	s	108	+++	R	0.05	13	+	+	n	3	0.12	n	RVH
16.	a.f.	110	+++	rs	0.04	1	−	−	——	——	——	——	B

n = no deviation; a.f. = auricular fibrillation; s = sinus.

TABLE III. ELECTROCARDIOGRAPHIC FINDINGS BEFORE AND AFTER COMMISSUROTOMY

CASES	(MONTHS)	QRS AXIS	CLOCK-WISE ROTATION	LEAD V_1			T WAVE		P WAVE		
				PATTERN	ACT. TIME (SEC.)	R/S (RATIO)	V_1	DIII	AXIS	AMPL.	DUR. (SEC.)
4. Before		75	+++	rS	0.06	0.3	−	−	n	2	0.12
After	7	30	++	rS	0.03	0.5	−	+	n	3	0.12
5. Before		10	+	rS	0.02	0.3	+	+	n	1	0.12
After	12	−2	counter-clockwise rotation	rS	0.02	0.3	+	+	n	1	0.08
6. Before		120	+++	R	0.03	5	−	−	right	5	0.12
After	2	108	+++	R	0.03	3	−	−	right	3	0.12
	4	108	++	rS	0.02	0.1	−	−	right	3	0.12
	7	98	++	rS	0.02	0.2	−	−	right	3	0.12
	17	70	+	rS	0.02	0.5	−	−	n	1.5	0.12
7. Before		74	+	RS	0.03	1.3	−	−	right	1.5	0.08
After	2	48	counter-clockwise rotation	RS	0.03	0.6	+	+	n	1	0.08
8. Before		105	+	Rs	0.04	8	+	+	n	0.5	0.08
After	2	98	+	Rs	0.04	1.3	+	+	left	0.5	0.08
	9	70	+	rS	0.03	0.3	+	+	left	1	0.08
9. Before		106	+++	qR	0.05	20	−	−	right	4	0.14
After	1	99	++	qRs	0.04	4	−	+	right	2	0.14
	7	100	+	Rs	0.04	4	−	+	right	3	0.14
11. Before		135	+++	R	0.06	8	−	−	These cases had auricular fibrillation.		
After	2	115	++	R	0.04	3	−	−			
15. Before		108	+++	R	0.05	13	+	+	n	3	0.12
After	2	100	++	RS	0.04	4	−	+	n	3	0.12

n = no deviation.

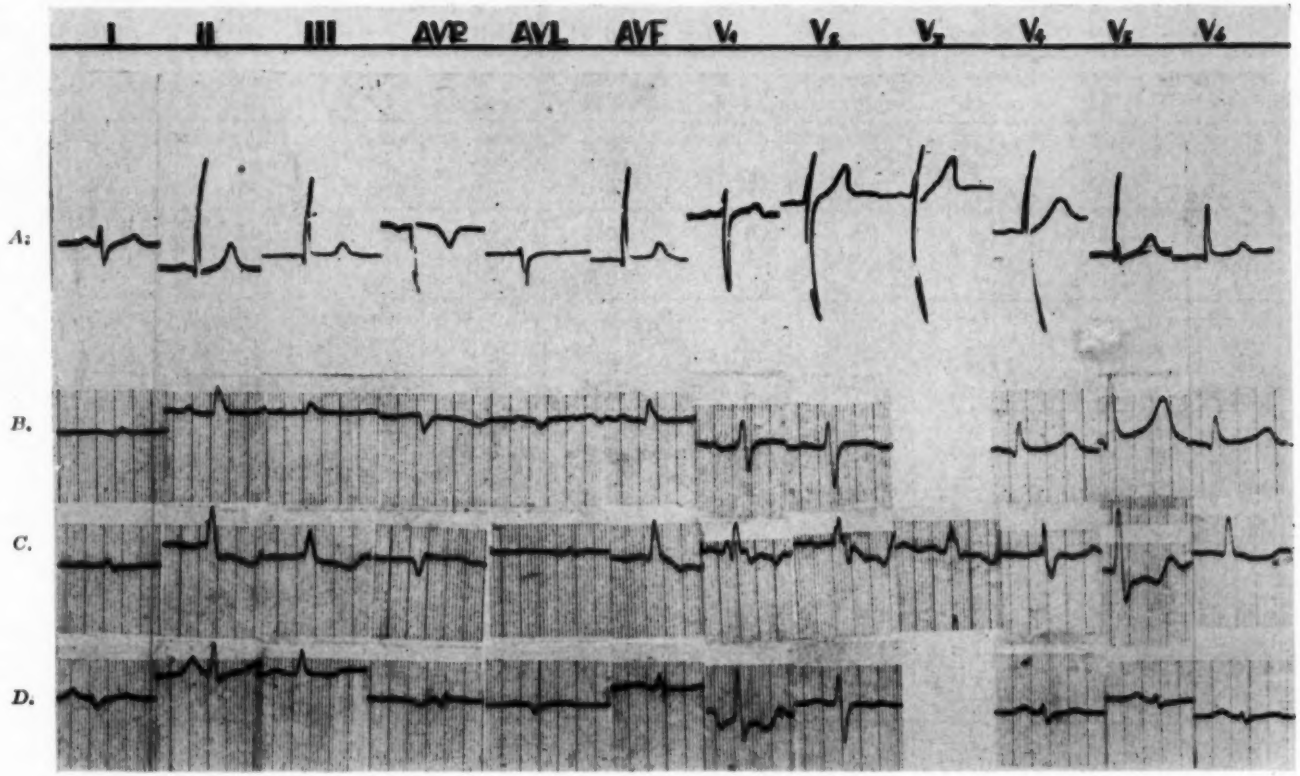

Fig. 1.—The four types of ventricular pattern found in mitral stenosis before commissurotomy. *A*, normal pattern, *B*, borderline, *C*, right bundle branch block, *D*, ventricular hypertrophy pattern.

In all the electrocardiographic tracings the following have been determined: deviation of QRS axis, degree of clockwise rotation, form of the ventricular complex in Lead V_1, activation time in Lead V_1, value of the R/S ratio in Lead V_1, direction of T wave of Leads V_1 and III, axis, height, direction and form of the auricular complex (Table II). All these cases have also been studied through postoperative serial tracings (Table III).

RESULTS

Auriculogram.—Among the sixteen cases, four were in auricular fibrillation; in the twelve remaining cases, the pattern of the P wave could be studied.

The P wave (Table II) was abnormal in duration or height in nine of the twelve cases. In three cases the P wave showed an abnormal morphology with splitting, notching, or a flat surface aspect by the standard leads. The axis of the P wave did not appear deviated in seven of the twelve cases, but was deviated toward the left in two cases and toward the right in three cases.

Relating these data with the hemodynamic pattern, we see that the three cases with normal P waves had a mitral surface area larger than 1 cm., except one case that had an area of 0.9 cm., and this case had a right ventricular hypertension of 90 mm. Hg. The other cases had no hypertension.

We have not found any relation between the presence of alterations in the form of the P wave, in the sense of splittings, notching, or flat aspect in the standard leads in patients with right ventricular and pulmonary hypertension, as in patients with normal pressures.

The form of P waves in Lead V_1 has been especially interesting, showing itself modified, except in the cases with slight mitral stenosis. In almost all cases a positive-negative diphasism of P wave was observed in this lead, even in those in which its aspect was normal by standard leads. The terminal negativity depends on the left auricular activation vector, which departs from the exploring electrode, being the more accentuated, the greater the left auricle dilatation is.

The deviation toward the left of the P-wave axis appears in two cases without pulmonary hypertension, while the cases with right P-axis deviation had pulmonary and right ventricular hypertension.

The P wave appeared with a high voltage in six cases; all but one had pulmonary hypertension. In all cases in which the right ventricular hypertension was superior to 40 mm. Hg, the P wave appears with a high voltage, except in two cases.

The most constant sign of abnormality of the P wave consists in its increased duration. This exceeded the 0.10 sec. in nine cases. In two of these nine cases no pulmonary hypertension was present.

Ventriculogram.—We have classified the ventriculogram in our cases into four types: normal, border line, right bundle branch block, and right ventricular hypertrophy pattern (Fig. 1).

We have considered "normal" those cases which did not present a delay in activation time, nor an inversion of the normal R/S ratio in Lead V_1, even when they presented a deviation toward the right of the axis and a certain degree of clockwise rotation. As "border line" we considered those cases in which there was a slight delay of activation time in Lead V_1 or a R/S ratio close to the unity with no or only slight delay in activation time in Lead V_1. In "right bundle branch block" we have included these cases with a double positivity in Lead V_1 accompanied by a delay in the ventricular activation time. Finally, we have considered as "right ventricular hypertrophy pattern" those tracings which presented a clear inversion of the normal R/S ratio in Lead V_1 accompanied by a clear delay in ventricular activation time.

The ventriculogram has been considered as normal in three cases. One of them had slight and well tolerated mitral stenosis. This case and another one presented no degree of pulmonary hypertension. The other case had a slight pulmonary hypertension which did not reach the level of 60 mm. Hg for systolic pressure. The two borderline cases had also only a slight pulmonary hypertension which did not exceed the systolic pressure level of 60 mm. Hg.

In both cases with right bundle branch block, the pulmonary systolic pressure did not exceed the 60 mm. Hg level. According to what we have seen in other cases, the right bundle branch block can appear at all pressure levels, but when the pulmonary and right ventricular pressures reach certain levels, a mixed pattern appears with both hypertrophy and right bundle branch block. The right ventricular hypertrophy pattern is shown by the unusual height of the second R wave[1] in Lead V_1.

In the nine cases with right ventricular hypertrophy pattern, the right systolic ventricular pulmonary pressure was greater than 60 mm. Hg, in most cases higher than 90 mm. Hg. Altogether the right ventricular hypertrophy pattern appeared more accentuated in relation to the degree of pulmonary and right ventricular hypertension.

MODIFICATIONS AFTER THE COMMISSUROTOMY

Of the sixteen cases studied, in one-half of them the electrocardiographic modification could be studied after the operation by means of serial tracings (Table III).

Auriculogram.—Except in one case with auricular fibrillation, all these cases had sinus rhythm before the commissurotomy. The auricular fibrillation appeared frequently (3 cases) during the postoperative period. It made its appearance generally after the third to the sixth day. In all cases it disappeared spontaneously without quinidine treatment, within the first month after the operation.

In the seven cases operated on with sinus rhythm, only two cases had a normal P wave. This normal aspect of P wave remains unmodified after operation. In the five remaining cases, the P wave remained unchanged in one case. It is interesting that the surgeon was not satisfied with the commissurotomy performed on this patient. In the four remaining cases the P wave changed

during the period that followed the commissurotomy. The height of the P wave diminished in two cases, both with pulmonary hypertension before the operation. In one of them the amplitude of P wave became completely normal. The diphasism of the P wave in Lead V_1 diminished in one case, and in two it disappeared completely. The abnormal duration of the P wave remains the same in three of the four cases.

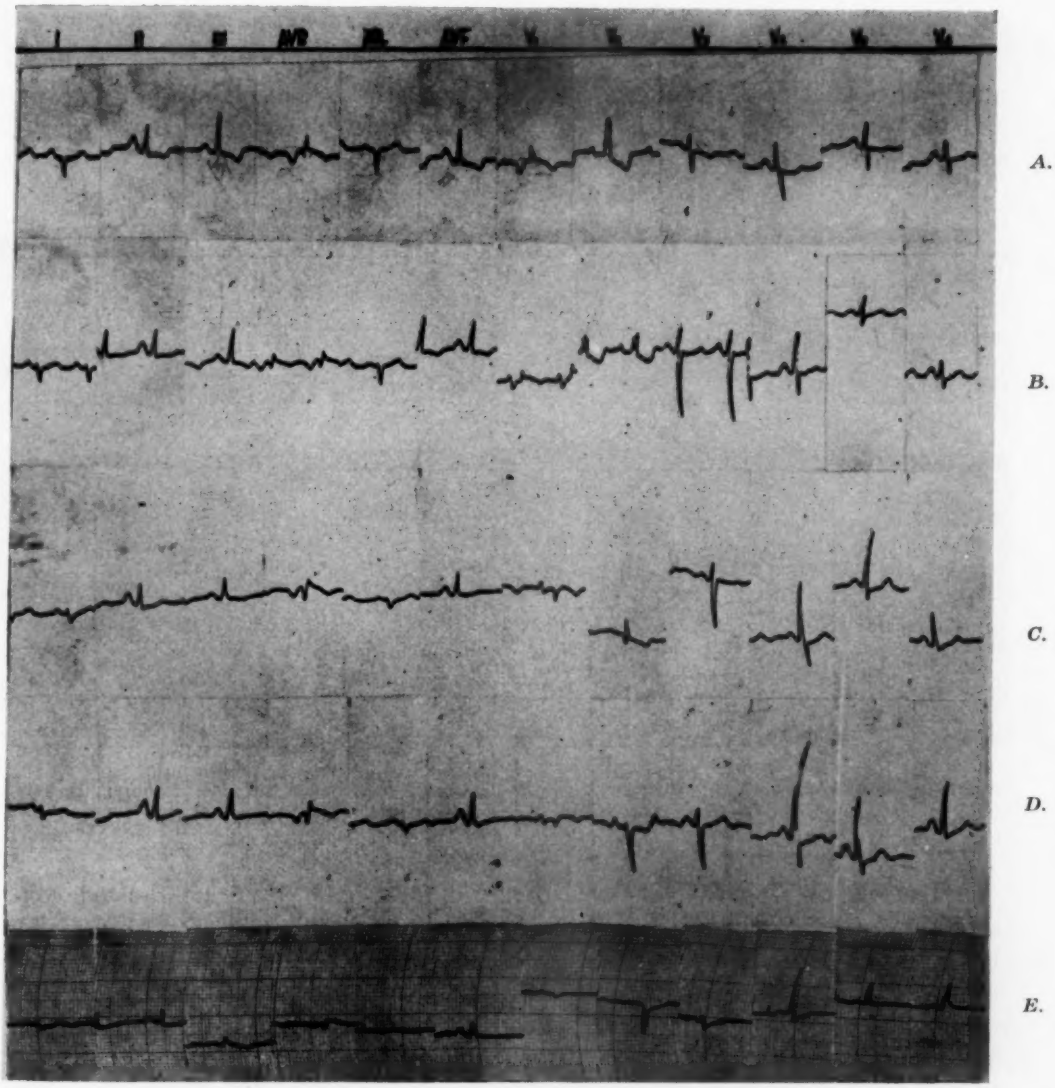

Fig. 2.—Pre- and postoperative electrocardiograms in Case 6. *A*, Before commissurotomy. *B, C, D, E*, Two, four, seven, and seventeen months after commissuorotmy, respectively.

Altogether, the P wave does not modify itself in its duration and morphologic aspects. The high voltage of P wave with an axis deviation toward the right, which we see in patients with great pulmonary hypertension is the sign that appears most usually, in an approach to normal. Frequently the negative component of P wave in Lead V_1 is also reduced.

Ventriculogram.—From the eight cases we followed after commissurotomy, one case exhibited a normal ventriculogram before the operation, another one had borderline ECG, and the other six showed a marked right ventricular hypertrophy pattern.

The case with a normal ECG remained normal after the commissurotomy, although with slight modifications for the sense of rotation around the longitudinal axis; from a slight clockwise rotation it has changed into a slight counterclockwise rotation one year after the operation.

The case with borderline ECG shows after the commissurotomy a diminution of the height of the R wave in Lead V_1, with a reduction of the R/S ratio and the disappearing of its slight clockwise rotation which has changed into a slight counterclockwise rotation.

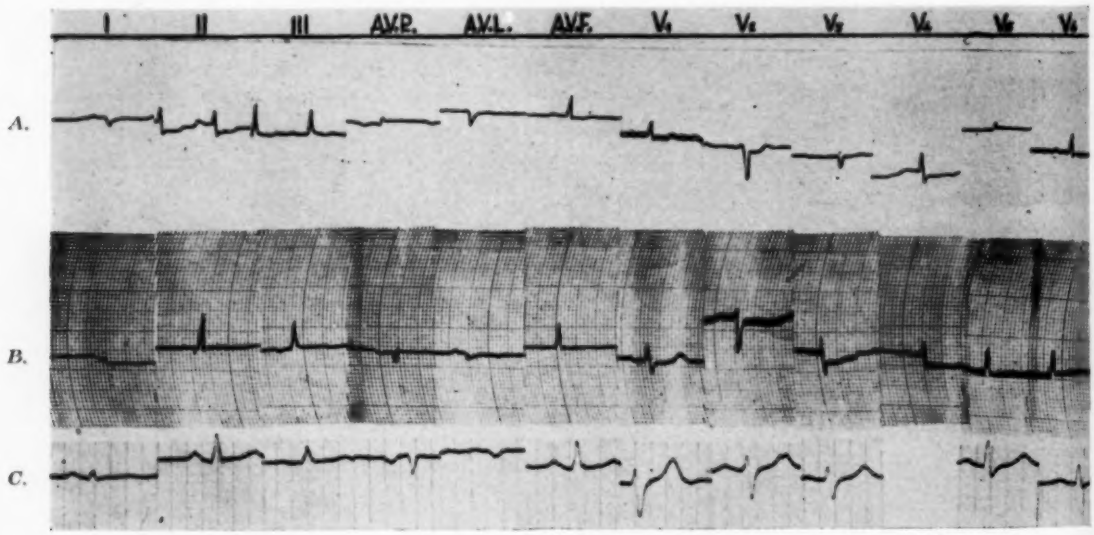

Fig. 3.—Pre- and postoperative electrocardiograms in Case 8. *A*, Before commissurotomy. *B*, Two months after commissurotomy. *C*, Nine months after commissurotomy.

The six cases with right ventricular hypertrophy patterns showed considerable postoperative changes. In one case, with the longest postoperative time, there was observed a regression of the right ventricular hypertrophy pattern, which disappeared completely within one and one-half year after the commissurotomy. In another case which showed an inversion of R/S ratio and a delay of activation time of 0.06 sec. in Lead V_1, these alterations returned to normal in 7 months after the commissurotomy (Fig. 2). In another case the right ventricular hypertrophy pattern disappeared within 9 months after the operation leaving only a QRS-axis deviation toward the right with a slight clockwise rotation (Fig. 3). In another case in 2 months after the commissurotomy it showed a diminution of the right ventricular hypertrophy pattern with a reduction of the R-wave height in Lead V_1, and changing of the R pattern into RS in this lead.

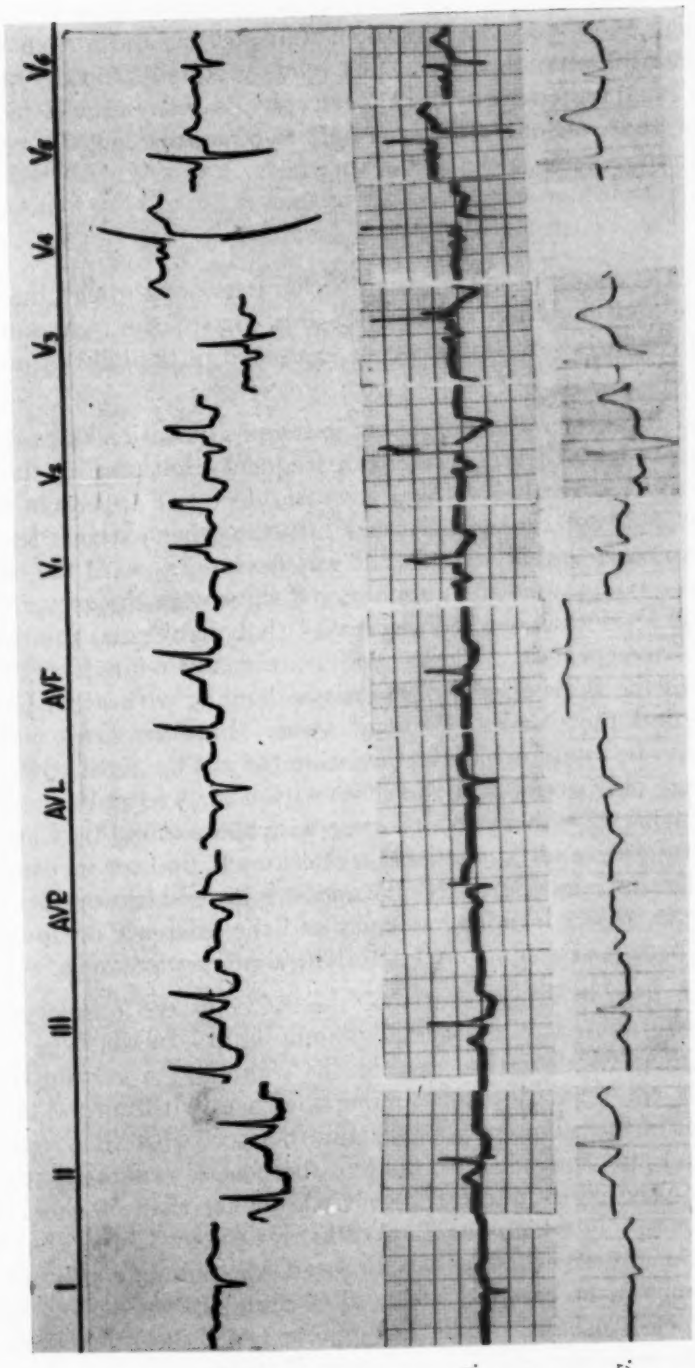

Fig. 4.—Pre- and postoperative electrocardiogram in Case 9. *A*, Before commissurotomy. *B*, One month after commissurotomy. *C*, Seven months after commissurotomy.

In the remaining two cases the inversion of the normal R/S ratio and the delay of activation time in Lead V_1 reached their normality quite clearly. One of them had a high pulmonary hypertension, that possibly did not yet reach its normal level 7 months after operation, but tends gradually toward normality, and it shows a gradual regression of the hypertrophy pattern in the ECG (Fig. 4). In the other case, that was operated upon only two months ago, the ventricular hypertrophy pattern remains, although less marked.

DISCUSSION

The classic ECG aspect of mitral stenosis characterized through the presence of mitral P wave and deviation of the QRS-axis toward the right and with a certain degree of clockwise rotation must be examined in the light of new hemodynamic knowledge.

The so-called P-mitral wave, consisting in its axis deviation toward the left, its duration superior to 0.10 sec. and with a frequent diphasism or flat surface aspect without any exaggerated voltage increase, does not appear in all cases. We found it only in 30 per cent of our cases. In the other patients the P wave was normal in two cases and in the other it was deviated toward the right with a high voltage, simulating more the pulmonary P wave with the exception of the diphasism in Lead V_1 with a marked negativity that manifested the role of the left auricle in P-wave genesis. These results are easily related to the hemodynamic data. In the cases of mitral stenosis without or with slight pulmonary hypertension we find the classical P-mitral wave. In some cases, however, a normal P wave may be found, while the deviation toward the right of the P wave with a high voltage only appears in the cases with a marked pulmonary hypertension. In a general way, these results agree with those found by Carouso and co-workers[2] and by Joly and co-workers.[3] The former find an incidence of P-mitral wave similar to ours (34 per cent) and the latter also found a relation between the P-wave aspect in mitral stenosis and the existence or not of a gradient of pressure between capillary and arterial pulmonary pressure.

As for the ventriculogram, aspects of the ECG in the four types found may be analogically related to the hemodynamic data. In the type we name "normal" with QRS-axis deviation toward the right and a certain degree of clockwise rotation, we found this only among the cases with normal or slightly increased pressures of the pulmonary artery and therefore with little repercussion to the work of the right ventricle. In none of these cases was the systolic pressure of the pulmonary artery and right ventricle higher than 50 mm. Hg. In the "borderline" cases, in which the R/S ratio was about 1, and the delay of activation time did not exceed 0.04 sec. in Lead V_1, pulmonary hypertension was present, although in no case did it exceed 60 mm. In the cases with "right bundle branch block", usually of the incomplete type, the pulmonary artery and right ventricle pressure were in our cases of different levels, but without exceeding 60 mm. Hg. Cosby and co-workers[4] found the right bundle branch block at all pressure levels, which we have comfirmed,[1] although when the pulmonary hypertension is much elevated, the unusual height of the second R wave in Lead V_1 means ventricular hypertrophy.

If the aspect of the P wave can serve us for an orientation of the degree of pulmonary hypertension, then, in our opinion, the aspect of the ventriculogram is still of great value. In none of our cases, that exhibited a clear pattern of right ventricular hypertrophy in Lead V_1, was the pulmonary systolic and right ventricular pressure below 60 mm. Hg. Gordon and co-workers[5] found in 1951 a relation between the hypertension of the right ventricles and the ECG pattern in congenital heart diseases. These results agree partly with those of Cosby and co-workers,[4] who found a normal ECG pattern or a borderline one, whenever the average systolic pressure of the pulmonary artery does not exceed 60 mm. Hg. As for the hypertrophy pattern, in spite of meeting it in some cases with a pressure lower than 60 mm. Hg, in most of the cases it only appears when the pulmonary pressure surpasses this level.

After the commissurotomy the study of the modifications of the ECG tracings is interesting. Besides the frequent appearance of auricular fibrillation during the postoperative course, which is generally transitory and disappears spontaneously, a study of the behavior of the P wave and the ventricular complex is of great interest. The P-mitral wave modifies itself rarely, except the diminution of the negative compound in Lead V_1, which, however, does not always manifest itself. The duration of the P wave will remain the same. The most important modifications appear in the type of P wave that accompanies the high pulmonary hypertensions. The voltage decreases in the following tracings. Joly and co-workers[3] have confirmed that there is a relation between these modifications of the P wave and the hemodynamic changes after the commissurotomy. Other authors[6] have observed some changes in the P wave after the operation, although there is no uniform judgment of their meanings.

Taking into account the relation between the form of ventriculogram and the pressure level in the pulmonary artery and the right ventricle, one can see that the first is modified according to the hemodynamic changes which take place on suppressing the mitral obstacle. The study of the ventriculogram has its real value in those cases of mitral stenosis, which have a higher gradient between arteriolar and capillary pulmonary pressures. Hereby, the observation of serial ECG records allows us nearly to follow the course of hemodynamic modifications until its complete disappearance. In the other types of ventriculogram, postoperative observation is much less interesting, as besides a diminution of the QRS axis toward the right and the degree of diminution of clockwise rotation, no other important modifications are observed.

SUMMARY AND CONCLUSIONS

A comparative study of the ECG and the hemodynamic data has been made in sixteen cases of mitral stenosis. In eight of them the ECG variations have been followed after commissurotomy until a maximum of one and one-half years.

Of twelve cases with sinus rhythm, the P wave was abnormal in nine cases before the intervention. In the remaining four cases auricular fibrillation was present. The most important sign of P-wave alteration consists in the increase of its duration over 0.10 sec., which appeared in the nine cases. Another important sign is the positive-negative diphasism of the P wave in Lead V_1.

The P wave had a high voltage in six cases, all but one had pulmonary hypertension. The P-wave axis was deviated in five cases. The two cases with a deviation toward the left were not accompanied by pulmonary hypertension, while the three cases with deviation toward the right had pulmonary and right ventricular hypertension.

The aspect of the ventriculogram before the operation was classified in four types: normal, border line, right bundle branch block, and right ventricular hypertrophy pattern. The normal, border line, and right bundle branch block tracings appear in the patients without or with a slight pulmonary hypertension, although the right bundle branch block can also be found in patients with a marked pulmonary hypertension. The tracings with a definite right ventricular hypertrophy pattern appear only when there is a marked pulmonary and right ventricular hypertension. In our cases they appear when the pulmonary systolic pressure is above 60 mm. Hg.

After the operation, a transitory appearance of auricular fibrillation was observed in three of eight cases. It appeared generally between the third to the sixth day and disappeared spontaneously in our cases before the first month.

The P wave usually modifies itself a short time after the operation, except the high voltage P wave with axis deviation toward the right and the reduction of the negative component of P wave in Lead V_1. The first is in relation to the reduction of pulmonary hypertension and the second according to the size of the mitral surface area.

As for the ventriculogram, in the six cases with right ventricular hypertrophy pattern, this disappeared completely in two cases, in the other four the inversion of the R/S ratio and the delay of activation time in Lead V_1 were less marked by the following ECG.

According to our judgment, the ECG examination constitutes a very valuable element in the study of the pre- and postoperative cases of mitral stenosis.

SUMMARIO IN INTERLINGUA

Esseva executate un studio comparative de hemodynamica e electrocardiographia in 16 casos de stenosis mitral. In 7 de iste casos le variationes electrocardiographic postcommissurotomic esseva observate pro 18 menses.

Ante commissurotomia mitral le constatationes electrocardiographic non es de accordo con le reduction del area valvular sed con le grado de hypertension pulmonar. Con pressiones pulmonar infra 60 mm Hg, le electrocardiogramma poteva esser normal o al limite inter normal e anormal. Con pressiones pulmonar supra 60 mm Hg, le electrocardiogramma poteva indicar hypertrophia dexteroventricular. Configurationes de bloco de branca dextere occurre con omne nivellos de pression.

Le efficacia de commissurotomia pote esser evalutate super le base de modificationes in le configuration electrocardiographic. Le configuration de hypertrophia dexteroventricular poteva esser reimplaciate per un configuration normal 6 menses post le commissurotomia.

Le unda P pote esser normal in casos de stenosis mitral. Su largor pote augmentar se sin relation a hypertension pulmonar, sed un augmentate voltage del unda P esseva observate exclusivemente in casos de alte pression pulmonar.

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A STUDY OF BLOOD PRESSURE IN RELATION TO DIET IN CHINESE AND CAUCASIAN STUDENTS IN NEW YORK CITY

FRANK W. LOWENSTEIN, M.D.*

NEW YORK, N. Y.

BLOOD pressure levels are influenced by diet, an important extrinsic factor. Evidence for this influence comes mainly from the treatment of hypertension by various dietary regimens over the past forty years.[1-6] It was not known, however, whether apparently healthy people, comparable in other important aspects (such as age, sex, race, and socioeconomic status) but eating different diets, would also show this influence of diet on their blood pressure levels.

In a previous paper[70] the author reviewed sixty-three papers appearing in the medical and anthropological literature of the last forty-five years, dealing with blood pressure measurements in Chinese and American people,[7-21] in relation to diet and blood pressure[22-39] and some constitutional factors such as weight, height, body build, and blood pressure.[40-69]

From this review it became apparent that roughly comparable groups of Chinese students[7-17] in China had a considerable lower blood pressure than Caucasian students in the United States.[18-21] There was some suggestive evidence that differences in diet may affect blood pressure levels in a few highly selected groups.[22-25] Furthermore, there were some indications that such intrinsic factors as weight and body build have a bearing on blood pressure. None of these tentative conclusions, however, was supported by sufficient evidence. Therefore, answers were sought to these questions.

1. Do comparable groups of Chinese have significantly lower blood pressure than Caucasians?

2. Do differences in diet account for differences in blood pressure, if any, between such groups?

3. What other factors may play a role in determining differences in blood pressure, if any, in these two racial groups?

SELECTION OF SUBJECTS

The subjects selected for this study were Chinese and Caucasian students from 20 to 45 years of age enrolled in one of the colleges in New York City. The Caucasian students were not limited as to their country of origin. The Chinese

From the Columbia School of Public Health, New York City.

This work was supported by a grant from the Milbank Memorial Fund, New York City.

Received for publication June 28, 1954.

*The data presented in this paper represent partial fulfillment of the requirements for the degree of Doctor of Public Health at the Columbia School of Public Health.

were required to be natives of China or some neighboring country, such as Korea or Indochina. American-born Chinese were purposely excluded from the study because they are known to differ in important aspects such as weight, body build, and mental attitude from the Chinese born in the Orient.[40] Any subject with a history and definite clinical signs and symptoms of hypertension was excluded from the study. Diet was made the main variable among the Chinese students; thus, they were divided into three groups: I. Chinese on a Chinese-type diet, II. Chinese on a mixed-type diet (50 per cent Chinese, 50 per cent American-type diet), and III. Chinese on an American-type diet. Group IV were Caucasians on an American-type diet.

A total of 262 subjects, 180 males and 82 females, were studied. Their average ages and sex distribution are presented in Table I.

TABLE I. MEAN AND STANDARD DEVIATION OF AGES FOR 262 MALE AND FEMALE STUDENTS IN FOUR STUDY GROUPS

GROUP	MALE (TOTAL 180)			FEMALE (TOTAL 82)		
	NO.	MEAN AGE IN YEARS	STANDARD DEVIATION	NO.	MEAN AGE IN YEARS	STANDARD DEVIATION
I	32	33.0	5.2	17	31.0	4.6
II	40	29.5	7.4	16	28.0	3.6
III	38	31.0	7.5	19	28.0	4.0
IV	70	29.0	5.0	30	29.0	6.9

METHODS

The following data were collected on each individual: (a) data on the medical history of each subject as gathered on the Cornell Medical Index, (b) data on physical characteristics as found during the first examination and three successive rechecks over a period of one year. Included were five blood pressure readings at each examination, taken on the right arm with the same mercury sphygmomanometer, usually during the evening between 7:00 and 10:00 P.M. in the following sequence: first reading, sitting; second, third, and fourth readings, lying down; and fifth reading, sitting again. Only two of these five readings were used for tabulation and analysis: the initial and the lowest readings. If the initial reading happened to be the lowest (which happened only occasionally) the second lowest reading was selected as the lowest for analysis. The auscultatory method was used; the systolic pressure being read at the point of reappearance of the first clear sound after inflation of the cuff well above the level of disappearance of all sounds, the diastolic pressure at the fourth phase where the clear sound changes to a muffled one. Each individual was asked not to eat for two hours before the examination because of the known influence of meals on blood pressure.

During the first physical examination particular attention was paid to the cardiovascular-renal system in order to exclude any apparent illness or defect of

this system. Vasomotor instability was measured in a very rough, semiquantitative way: cold hands or feet during one examination, Grade 1; cold hands and feet during one examination or cold hands or feet during repeated examinations and also answered questions 37, 74, and 75 on the Cornell Medical Index Health Questionnaire with "yes," Grade 2; if all signs mentioned under 2 were present, plus other signs of vasomotor instability, such as positive dermographism, it was rated Grade 3. Careful measurements of weight, height, and chest circumference were taken on each individual, the weight measurements being repeated at each successive examination. (c) Data on the dietary intake of each individual, as collected from a two-day diet record; in addition, data on the dietary history of each Chinese, as taken on the weekly food inventory with data on their intake in 1938, 1943, and 1953.

RESULTS

The data on physical characteristics constitute the most important ones for analysis, while the data on the medical history and the dietary intake may be looked upon as supplementary to the former.

Dietary Findings.—The dietary data were used only to determine to which group each individual belonged. This presented no problem in the Caucasian group; however, in the Chinese it required the setting up of definite criteria for each group. In Table II, an attempt has been made to semiquantitate the average weekly intake of the main foods used in each group.

TABLE II. MAIN FOODS AND THE APPROXIMATE WEEKLY AMOUNT USED BY THREE GROUPS OF CHINESE STUDENTS

FOOD USED	CHINESE GROUPS		
	GROUP I CHINESE DIET	GROUP II MIXED DIET	GROUP III AMERICAN DIET
Rice	14 or more bowls	2-14 bowls	1-2 bowls
Wheat bread, white or wholewheat	7 slices or less	7 slices or more	More than 14 slices
Pork	3-4 pounds	1-3 pounds	Less than 1 pound
Beef	Less than 1 pound	1-2 pounds	2-4 pounds
Lard	7-14 tablespoons	3-7 tablespoons	Less than 3 tablespoons
Butter or margarine	1 tablespoon or less	1-2 tablespoons	More than 2 tablespoons
Soy sauce	3 ounces or more	1-3 ounces	Less than 1 ounce
Milk	Less than 2 cups	2-4 cups	4-7 cups
Coffee	None	2-5 cups	5-10 cups

From this table it becomes apparent that rice was the main carbohydrate in Group I, while wheat served as the main carbohydrate in Group III, similar to the Caucasian Group IV. Pork was the main meat protein in Group I while beef was in Group III, again similar to Group IV. Lard was the main source of fat used in Group I, mainly for cooking, whereas butter or margarine served as the main source of fat in Group III. Group I consumed negligible amounts of

milk while Group III used amounts comparable to low milk-consuming groups in this country. Coffee was not used in Group I, Chinese tea being their main beverage, while Group III used a fair amount of coffee. Group II was intermediate in the intake of all these foods mentioned. Group I was distinguished further by the fact that most of the meals were prepared at home in Chinese style, while more than 50 per cent of the meals eaten by Groups II and III were restaurant and cafeteria meals. Thus, it is apparent that there were considerable differences, both as to qualitative and quantitative nature of the diets of the three Chinese groups, particularly between Groups I and III. Group IV, the Caucasian, was similar to Group III but consumed more calories.

TABLE III. MEAN AND STANDARD DEVIATIONS OF HEIGHTS FOR 262 MALE AND FEMALE STUDENTS IN FOUR STUDY GROUPS

GROUP	MALES (TOTAL 180)			FEMALES (TOTAL 82)		
	NO.	MEAN HEIGHT (INCHES)	STANDARD DEVIATION	NO.	MEAN HEIGHT (INCHES)	STANDARD DEVIATION
I	32	66.5	2.8	17	61.3	1.5
II	40	66.2	2.0	16	62.0	2.0
III	38	65.9	2.6	19	62.1	1.8
IV	70	68.9	2.7	30	64.0	2.2

TABLE IV. MEAN AND STANDARD DEVIATIONS OF WEIGHTS FOR 262 MALE AND FEMALE STUDENTS IN FOUR STUDY GROUPS

GROUP	MALES (TOTAL 180)			FEMALES (TOTAL 82)		
	NO.	MEAN WEIGHT (POUNDS)	STANDARD DEVIATION	NO.	MEAN WEIGHT (POUNDS)	STANDARD DEVIATION
I	32	135	9	17	107	4
II	40	136	20	16	107	10
III	38	134	19	19	109	11
IV	70	164	19	30	125	11

Physical Findings.—A comparison of the heights, weights, and chest circumferences of the four study groups showed the only significant* differences between Caucasians in Group IV and the Chinese in Groups I to III.

The measurements for the Chinese males and females in all three groups were almost identical.

*Throughout this study a difference is considered statistically significant if the probability of exceeding this difference is less than 1 per cent, of borderline significance if the probability of exceeding it is between 1 per cent and 5 per cent, and as not significant if the probability of exceeding it is more than 5 per cent.

TABLE V. MEAN AND STANDARD DEVIATIONS OF CHEST CIRCUMFERENCES FOR 262 MALE AND FEMALE STUDENTS IN FOUR STUDY GROUPS

GROUP	MALES (TOTAL 180)			FEMALES (TOTAL 82)		
	NO.	MEAN CHEST CIRCUM-FERENCE	STANDARD DEVIATION	NO.	MEAN CHEST CIRCUM-FERENCE	STANDARD DEVIATION
I	32	33.5	1.7	17	31.3	1.9
II	40	34.0	2.1	16	31.0	2.1
III	38	33.9	2.8	19	31.4	1.9
IV	70	37.4	1.4	30	32.9	0.9

A comparison of the amount of cardiovascular-renal disease in the parents of the individuals in the four study groups revealed some significant differences, as determined by the X^2 test among the males:

TABLE VI. PER CENT OF POSITIVE, NEGATIVE, AND QUESTIONABLE FAMILY HISTORIES OF CARDIOVASCULAR-RENAL DISEASE IN MALES AND FEMALES IN FOUR STUDY GROUPS

GROUP	MALES (TOTAL 180)				FEMALES (TOTAL 82)			
	PER CENT OF EACH STUDY GROUP				PER CENT OF EACH STUDY GROUP			
	NO.	POSITIVE	NEGATIVE	QUES-TIONABLE	NO.	POSITIVE	NEGATIVE	QUES-TIONABLE
I	32	25	56	19	17	47	47	6
II	40	40	50	10	16	50	50	0
III	38	16	76	8	19	47	47	6
IV	40	52	39	9	30	67	33	0

The Chinese in Groups I and III differed significantly from the Caucasians in Group IV; Group III, however, differed also significantly from Group II which differed neither significantly from Group IV nor from Group I. No significant differences were found among the females in any of the four groups.

In regard to the amount of various degrees of vasomotor instability present

TABLE VII. PER CENT OF MALES AND FEMALES SHOWING VARIOUS DEGREES OF VASOMOTOR INSTABILITY IN FOUR STUDY GROUPS

GROUP	MALES (TOTAL 180)					FEMALES (TOTAL 82)				
	PER CENT OF EACH STUDY GROUP					PER CENT OF EACH STUDY GROUP				
	NO.	GRADE 1	GRADE 2	GRADE 3	ABSENT	NO.	GRADE 1	GRADE 2	GRADE 3	ABSENT
I	32	13	3	0	84	17	0	29	0	71
II	40	15	10	0	75	16	6	19	0	75
III	38	5	9	0	86	19	11	5	0	84
IV	70	27	27	3	43	30	17	30	6	47

in the four groups, significant differences existed between the males in the three Chinese groups on the one hand and the Caucasian group on the other.

The males in the three Chinese groups showed no significant differences between each other. In the females there were no significant differences except between Groups III and IV; the differences between the females in Group II and IV were of borderline significance. In other words, the Caucasians in Group IV showed the highest degree and amount of vasomotor instability for both sexes, the Chinese in Group III the lowest degree, again for both sexes.

Before presenting a series of tables on mean blood pressures, it should be mentioned that in regard to the per cent of allergic manifestations present, all four groups showed a similar figure. The males in all four groups had less allergic manifestations than the females; Group III had the lowest per cent with 5 per cent in the males and 11 per cent in the females. None of the differences found between the four groups in either sex were statistically significant.

The same can be said regarding the socioeconomic status of the individuals in the four study groups. Every individual was classified either as totally self-supporting, partially self-supporting, or not self-supporting.

In regard to a few other items of potential importance to the problem under study, the four groups showed no significant differences in the following: (1) the presence or absence of true and questionable heart murmurs; (2) the presence or absence of kidney abnormalities; (3) the presence or absence of some chronic diseases, other than of the cardiovascular-renal system as judged from the physical examination and the medical history. The number of positive findings in any of these three categories was very small in any one of the four study groups.

The information obtained concerning the use of tobacco gave some indication as to how many students in each group smoked between ten and twenty cigarettes or more than twenty cigarettes daily. In the males, taking both categories of smokers combined, Groups I and IV differed significantly (6 per cent against 29 per cent). None of the other groups differed significantly from each other. In the females there were no smokers in Groups I and II, only in Group III, while Group IV had five, or 17 per cent.

The next series of tables contains mean blood pressure values, systolic and diastolic, two out of five readings taken: the initial (causal) and the lowest readings for all four groups during each of four successive periods.

TABLE VIII. MEAN BLOOD PRESSURES IN MM. HG FOR 262 FEMALES AND MALES IN FOUR STUDY GROUPS FIRST PERIOD (FEBRUARY-MAY)

STUDY GROUP	MALES (TOTAL 180)					FEMALES (TOTAL 82)				
	NO.	SYSTOLIC		DIASTOLIC		NO.	SYSTOLIC		DIASTOLIC	
		INITIAL	LOWEST	INITIAL	LOWEST		INITIAL	LOWEST	INITIAL	LOWEST
I	32	115.6	112.8	84.7	79.4	17	105.6	102.1	76.2	72.1
II	40	119.3	113.5	84.3	78.0	16	114.4	108.8	79.4	76.9
III	38	116.8	111.6	84.7	78.9	19	110.3	106.6	78.6	75.5
IV	70	125.9	121.1	89.1	84.7	30	114.3	107.7	79.3	72.3

It is apparent from Table VIII that the mean systolic and diastolic blood pressure in the males differs slightly in Groups I, II, and III, but markedly between each of these and Group IV which showed the highest average pressure in each category. The findings in the females revealed no marked difference between the four groups, except for the systolic pressures in Group I which were lower than those in the other three.

Table IX shows which of the differences found in comparing the mean blood pressure levels of two out of four groups were statistically significant. Significance was determined according to the normal curve test at the 0.01 level:

$$\sigma m_1 - m_2 = \sqrt{\sigma m_1^2 + \sigma m_2^2}$$

TABLE IX. SUMMARY OF SIGNIFICANCE OR NONSIGNIFICANCE OF DIFFERENCES FOUND IN MEAN BLOOD PRESSURE LEVELS IN MALES AND FEMALES OF FOUR STUDY GROUPS FOR THE FIRST PERIOD

GROUPS	MALES				FEMALES			
	SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC	
	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST
I & IV	+*	+	?†	+	+	?	0‡	0
II & IV	+	+	+	+	0	0	0	0
III & IV	+	+	?	+	0	0	0	0
I & II	0	0	0	0	+	?	0	0
I & III	0	0	0	0	0	0	0	0
II & III	0	0	0	0	0	0	0	0

*+Significant; † ? Borderline; ‡O Not significant.

Table X shows mean blood pressure levels for 209 females and males in the four study groups during the second check period.

TABLE X. MEAN BLOOD PRESSURES IN MM. HG FOR 209 FEMALES AND MALES IN FOUR STUDY GROUPS SECOND PERIOD (MAY-JULY)

STUDY GROUP	MALES (TOTAL 146)					FEMALES (TOTAL 63)				
	NO.	SYSTOLIC		DIASTOLIC		NO.	SYSTOLIC		DIASTOLIC	
		INITIAL	LOWEST	INITIAL	LOWEST		INITIAL	LOWEST	INITIAL	LOWEST
I	27	112.8	110.6	82.0	76.9	14	108.6	104.3	75.7	74.3
II	32	115.6	112.8	81.6	77.2	12	110.8	108.3	77.5	75.8
III	30	111.3	111.0	80.7	77.7	14	112.1	107.1	77.8	75.7
IV	57	118.0	117.1	81.9	78.0	23	106.3	102.3	72.8	68.5

A certain loss of subjects occurred in each group between the first and second period.

Table XI gives a summary of significance or nonsignificance of differences found in mean blood pressure levels in males and females of the four study groups.

TABLE XI. SUMMARY OF SIGNIFICANCE OR NONSIGNIFICANCE OF DIFFERENCES FOUND IN MEAN BLOOD PRESSURE LEVELS IN MALES AND FEMALES OF FOUR STUDY GROUPS FOR THE SECOND PERIOD

GROUPS	MALES				FEMALES			
	SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC	
	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST
I & IV	?†	+*	0‡	0	0	0	0	?
II & IV	0	?	0	0	0	0	0	+
III & IV	+	+	0	0	0	0	0	+
I & II	0	0	0	0	0	0	0	0
I & III	0	0	0	0	0	0	0	0
II & III	0	0	0	0	0	0	0	0

*+ Significant; †? Borderline significance; ‡O Not significant.

The differences found during the first period were still present during the second period, but less marked. All blood pressure levels showed a decrease as compared to the first period with the lowest levels reached in the females of Group IV.

Tables XII and XIII present mean blood pressure levels and the significance of the differences found for 178 subjects checked during the third period.

TABLE XII. MEAN BLOOD PRESSURES IN MM. HG FOR 178 FEMALES AND MALES IN FOUR STUDY GROUPS THIRD PERIOD (SEPTEMBER-NOVEMBER)

STUDY GROUP	MALES (TOTAL 119)					FEMALES (TOTAL 59)				
	NO.	SYSTOLIC		DIASTOLIC		NO.	SYSTOLIC		DIASTOLIC	
		INITIAL	LOWEST	INITIAL	LOWEST		INITIAL	LOWEST	INITIAL	LOWEST
I	23	107.6	105.0	77.2	74.1	12	100.8	100.0	73.3	70.8
II	26	114.6	110.8	79.2	77.3	11	103.2	102.3	73.2	71.3
III	23	111.5	107.2	77.6	74.1	12	106.6	103.3	76.6	70.0
IV	47	116.9	115.2	79.9	78.4	24	105.4	101.3	70.8	66.6

A further loss of subjects took place as compared to the second period except in the females of Group IV. The differences found during two preceding periods were present again and somewhat more marked than during the second period. A further decrease of all blood pressures was noted.

Tables XIV and XV present the results of the fourth and final check for 156 subjects in the four study groups.

TABLE XIII. SUMMARY OF SIGNIFICANCE OR NONSIGNIFICANCE OF DIFFERENCES FOUND IN MEAN BLOOD PRESSURE LEVELS IN MALES AND FEMALES OF FOUR STUDY GROUPS FOR THE THIRD PERIOD

GROUPS	MALES				FEMALES			
	SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC	
	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST
I & IV	+*	+	0‡	0	0	0	0	0
II & IV	0	0	0	0	0	0	0	0
III & IV	?†	+	0	?	0	0	?	0
I & II	?	?	0	0	0	0	0	0
I & III	0	0	0	0	?	0	0	0
II & III	0	0	0	0	0	0	0	0

*+ Significant; †? Borderline significance; ‡O Not significant.

TABLE XIV. MEAN BLOOD PRESSURES IN MM. HG FOR 156 FEMALES AND MALES IN FOUR STUDY GROUPS FOURTH PERIOD (NOVEMBER-JANUARY)

STUDY GROUP	MALES (TOTAL 108)					FEMALES (TOTAL 48)				
	NO.	SYSTOLIC		DIASTOLIC		NO.	SYSTOLIC		DIASTOLIC	
		INITIAL	LOWEST	INITIAL	LOWEST		INITIAL	LOWEST	INITIAL	LOWEST
I	20	107.0	107.0	76.0	74.5	12	102.5	102.5	73.3	70.8
II	25	112.2	109.0	76.2	74.6	10	106.0	101.0	74.0	71.0
III	21	110.2	107.4	75.9	75.9	10	104.0	99.0	72.0	71.0
IV	42	118.1	115.5	81.4	77.6	16	103.7	100.0	71.3	66.9

TABLE XV. SUMMARY OF SIGNIFICANCE OR NONSIGNIFICANCE OF DIFFERENCES FOUND IN MEAN BLOOD PRESSURE LEVELS IN MALES AND FEMALES OF FOUR STUDY GROUPS FOR THE FOURTH PERIOD

GROUPS	MALES				FEMALES			
	SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC	
	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST	INITIAL	LOWEST
I & IV	+*	+	?†	0‡	0	0	0	0
II & IV	+	+	+	0	0	0	0	0
III & IV	+	+	+	0	0	0	0	0
I & II	0	0	0	0	0	0	0	0
I & III	0	0	0	0	0	0	0	0
II & III	0	0	0	0	0	0	0	0

*+ Significant; †? Borderline significance; ‡O Not significant.

The differences encountered during three preceding periods became more pronounced again as compared to the second and third periods.

The results of the follow-up of the blood pressure in all those individuals who had complete checks throughout all four periods are presented in Figs. 1 and 2 for all four groups in each category.

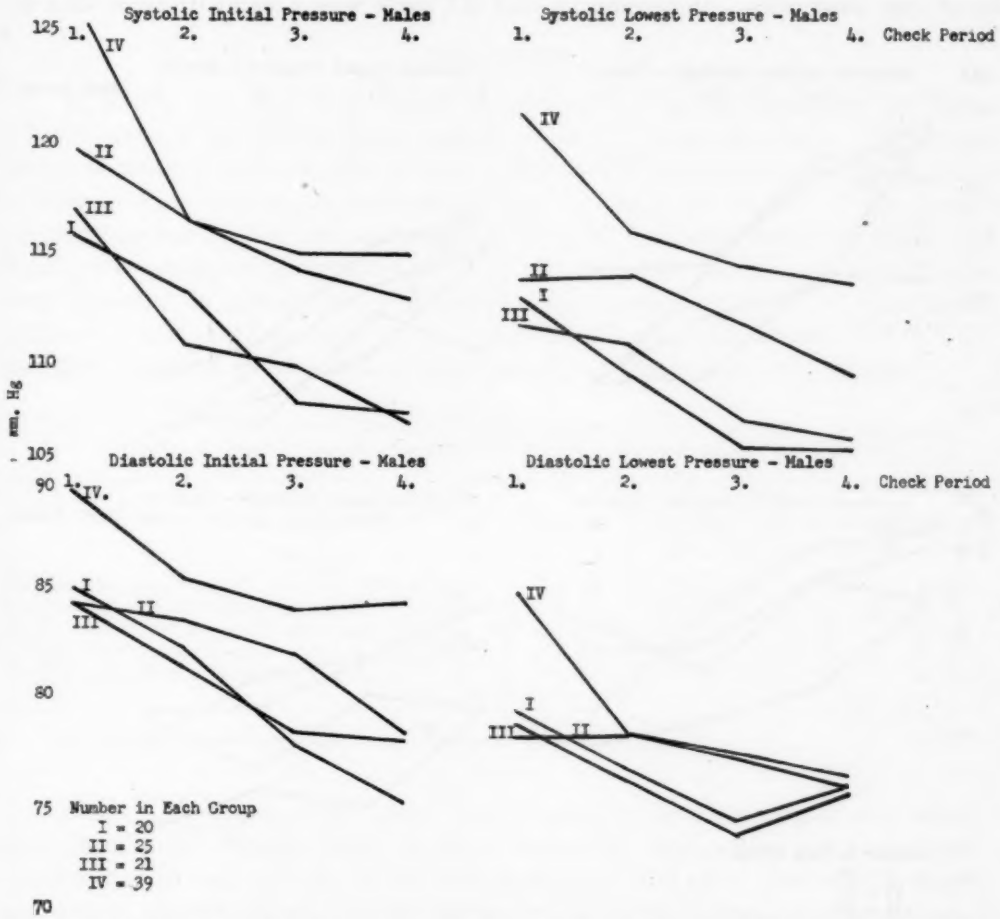

Fig. 1.—Follow-up of mean blood pressures (mm. Hg) throughout four successive periods (1, 2, 3, 4) over one year in males of four study groups (I, II, III, IV).

The statistical significance of the differences found between check periods in each group was determined again according to the normal curve test:

$$\sigma\Delta = \sqrt{\frac{\Sigma\,(\Delta)^2}{N} - m\Delta^2}$$

In the males the mean blood pressures in all four categories showed a decrease between the first and second period. This decrease reached significance in the Caucasian Group IV in all categories, in the Chinese Group III in the systolic initial, diastolic initial, and lowest categories. In Group I the fall of the mean pressures did not become significant until the third period, while in Group II it

took until the fourth period to show any significant decrease. In Groups I, III, and IV the mean pressures stayed either at the same level or showed a slight increase between the third and fourth period.

In the females the picture is somewhat different. Between the first and second period only Group IV showed a significant decrease of mean blood pressure in all four categories. In Groups II and III there was a slight decrease and in

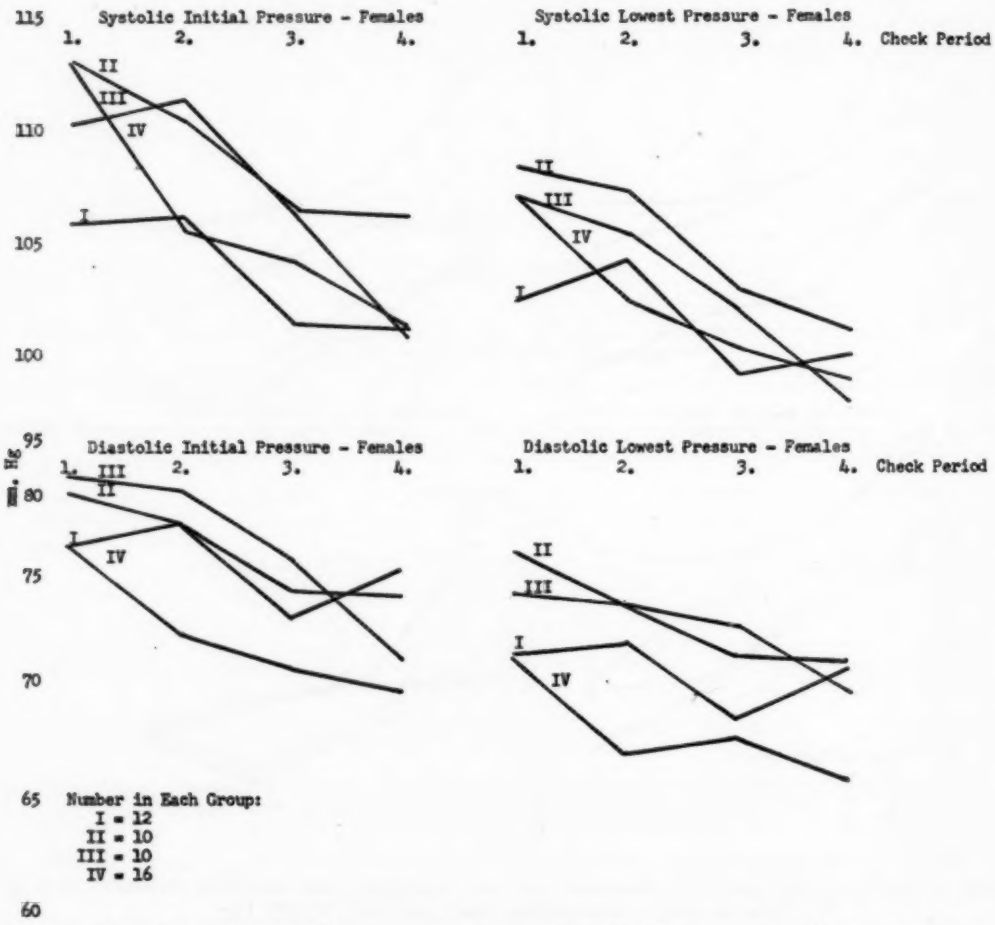

Fig. 2.—Follow-up of mean blood pressures (mm. Hg) throughout four successive periods (1, 2, 3, 4) over one year in females of four study groups (I, II, III, IV).

Group I even a slight increase. Between the second and third period, however, mean pressures showed a continuous fall in all four groups with Group IV reaching lower levels than the other three. Between the third and fourth period mean pressures in Groups III and IV continued to decrease slightly, whereas in Group II they were almost stationary and in Group I showed a slight increase.

A summary of the data on blood pressure as presented in the foregoing tables is shown in Figs. 1 and 2. They reveal between successive check periods a tendency to drop in all four categories for both sexes in all four groups. This

drop, however, occurred during different periods in the various groups: In the Caucasians of Group IV, it became significant during the second check period in both sexes, whereas in most of the Chinese in all three groups it did not reach significant levels until the third or fourth period; in other words, among the Chinese, except in the males of Group III, the decrease in mean pressures was slower and of slightly lower magnitude than in the Caucasians.

DISCUSSION

It seems apparent that significant differences existed between the three Chinese groups on the one hand and the Caucasians on the other. Among the physical characteristics, height, weight, and chest circumference were significantly smaller in the Chinese of both sexes than in the Caucasians. These results support the findings by previous investigators,[10,44,73] at least as far as weight and height are concerned (no reports on chest circumference measurement in Chinese were found). In connection with the findings of some authors[8,23,28] that blood pressure is positively correlated with weight and less so with height[16,24,28,31,32,35-37] the question arose whether this correlation existed in our four study groups.

TABLE XVI. CORRELATION COEFFICIENTS FOR HEIGHT, WEIGHT, SYSTOLIC LOWEST, AND DIASTOLIC LOWEST BLOOD PRESSURE IN THE MALES OF FOUR STUDY GROUPS

CORRELATION COEFFICIENT	GROUP I	GROUP II	GROUP III	GROUP IV
Height and weight	0.48	0.93	0.68	9.68
Height and systolic lowest pressure*	−0.13	−0.43	0	−0.78
Height and diastolic lowest pressure*	−0.42	−0.17	−0.37	0.17
Weight and systolic lowest pressure	0.29	0.44	0.32	−0.50
Weight and diastolic lowest pressure	0.25	0.22	0.14	0.39

*The measurements chosen are the ones taken at the first examination.

Table XVI shows clearly that the correlation between height and weight and systolic and diastolic blood pressure was either insignificant or negative in the males of all four groups. Thus, it becomes apparent that differences in height and weight cannot explain the differences found in blood pressure levels between the Chinese and Caucasians in the four study groups.

In the following an attempt will be made to analyze some of the differences found in mean blood pressures between the two racial groups and the two sexes. In a study of the males first, it was noted that the differences in mean blood pressures between the three Chinese groups and the Caucasian group were most marked during the first check period; they became less pronounced during the second and third check period and were more marked again at the fourth check. The explanation for this phenomenon may be found in the following: from the follow-up of the mean blood pressure in each group over one year it was observed that a significant fall took place in Group IV between the first and second check period, whereas in Groups I to III it did not reach significance at least until the third check period, with the exception of the diastolic pressures and the systolic

initial pressure in Group III. In other words, the three Chinese groups showed a definite time lag in their drop of mean pressure levels over one year as compared to the Caucasian group. This time lag explains why the differences in mean pressure levels between the Chinese groups and the Caucasian group became less marked during the second check period; after this time lag had ceased to operate during the third check period, differences between the Chinese and Caucasians became more marked again, and during the fourth period reached significance in all categories except the diastolic lowest pressures.

The findings presented by the females were quite different: only in a few instances did the differences found between the various groups reach significance; these significant differences existed between Groups I and IV in the systolic initial pressure, but also between Groups I and II during the first check period. In the second period significant differences were found between Groups II and IV, and III and IV in the diastolic lowest pressures only; at no other period were these differences significant. This phenomenon can be explained in a similar drop in mean pressure levels in all four groups over one year, but this drop occurred in Group IV during the second period while in Groups II and III it became marked only in the third period. Furthermore, the mean diastolic pressures in Group IV fell to lower levels than in any of the three Chinese groups. These two phenomena explain why the differences between Groups II and IV, and III and IV in the diastolic lowest pressures became significant during the second check period.

In trying to explain the changes of mean blood pressure over one year between different check periods, found in all four study groups, one thinks first of some extrinsic seasonal factor. If season was the only factor operating, all four groups should show similar changes at the same time, i.e., if blood pressures drop usually during the warm season, then this drop should have become manifest in all four groups during the second or at least during the third period. Obviously this was the case, with one exception, for the females in Group III, who did not show any marked drop in their pressures until the fourth period. If the change from the cold to the warm season was causing a fall in blood pressure, one would expect a rise again during the cold season. This rise did not take place, at least not to any significant extent, in any of the four groups. Therefore, the operation of a true seasonal variation in causing the previously mentioned changes becomes questionable.

An intrinsic factor which may have been operating is one of habituation: blood pressures were highest in all four groups during the first examination when each individual subject was confronted with a new situation, including the examiner ("the new doctor"). During the second and certainly during the third examination the situation was not new any longer and the relationship between each subject and the examiner was one of confidence. This factor is known to operate in general between the individual patient and his physician. There is no doubt that it also operated here. Why it should have worked slower in the Chinese than in the Caucasian cannot be answered.

By looking at the differences in mean blood pressure levels (Table XVII) between males and females in the same group, it is apparent that they differed significantly in most instances, with the differences being more marked in Group IV than in the three Chinese groups during all four check periods. This finding adds support to what has been considered as a well-established fact, that females during their reproductive period have significantly lower pressures than males.

In considering the significant differences in mean blood pressure levels within the same sex, only the males showed such differences between the two racial groups during all four check periods. It is true that the relatively small number of females makes the evaluation of this absence of any significant differences more difficult; it may be argued that a larger sample of females in each group might have shown similar differences as in the males; however, the fact that the mean pressures in the Caucasian girls of Group IV reached even lower levels during their drop between periods 1 and 2 than in any of the three Chinese groups, at any time, seems to make the afore-mentioned argument less valid. After having established the fact that the Chinese males in our three study groups did show significantly lower blood pressure levels, a fact which supports the findings by previous investigators,[7-17] one looks next for an explanation of this fact. Some of the constitutional factors such as weight and height have already been discussed and excluded as significant determinants of blood pressure levels in the four groups.

Two other factors deserve to be mentioned here as of possible significance: as was shown in Table VI, there was a marked difference in the per cents of positive family histories of cardiovascular-renal diseases between the males of the various groups. The lowest per cent was present in Group III followed by Groups I and II, while Group IV had the highest per cent. The differences between Groups III and IV, and I and IV were statistically significant.

One may rightly question the reliability of historic data of this kind, although they were double checked by personal questioning during the first examination. Differences in customs, regarding the frequency and quality of medical care and separation from their parents on the Chinese mainland for five or more years, are factors which may have influenced these data in the Chinese males in the direction of a lower per cent of cardiovascular-renal disease in their parents: however, one might have expected these same factors to operate in the females. That heredity plays its role in determining the blood pressure of the individual has been fairly well-established from studies on the increased familial occurrence of hypertension. It is interesting to note that the females did not show any significant differences in the per cent of positive family histories in each group; however, the differences between females and males in Groups I and III were significant. No explanation has been forthcoming for these last findings.

The second factor of importance here is the presence of vasomotor instability, as shown in Table VII. The picture here seems to be more clear-cut than in the family histories. All three male Chinese groups exhibited significantly less symptoms and signs of vasomotor instability than did the male Caucasians; there were also some differences among the females, reaching significance only

TABLE XVII. SHOWING DIFFERENCES IN MEAN BLOOD PRESSURE VALUES BETWEEN MALES AND FEMALES IN FOUR STUDY GROUPS FOR FOUR OBSERVATION PERIODS

DIFFERENCES BETWEEN MALES AND FEMALES IN MM. HG	GROUP I				GROUP II				GROUP III				GROUP IV			
	SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC		SYSTOLIC		DIASTOLIC	
	INIT.	LOW	INIT.	LOW	INIT.	LOW	INIT.	LOW	INIT.	LOW	INIT.	LOW	INIT.	LOW	INIT.	LOW
1. Obser.	10.0	11.0	8.5	7.3	4.9	4.7	4.9	1.1	6.5	5.0	6.1	3.4	11.6	14.4	9.8	12.4
2. Obser.	4.5	6.5	6.8	2.6	4.8	4.5	4.1	1.4	−0.5	3.9	2.9	2.0	11.7	14.8	9.1	9.5
3. Obser.	6.8	5.0	3.9	3.3	11.4	8.5	6.0	6.0	4.9	3.9	1.0	4.1	11.5	13.9	9.1	11.8
4. Obser.	4.5	4.5	2.7	3.7	6.2	8.0	2.2	3.6	6.2	8.4	3.9	4.9	14.4	15.5	10.1	10.7

between Groups III and IV. Whether this apparent correlation between vasomotor instability and blood pressure levels in these four study groups was also a causal relationship will not be discussed here because of the various other factors (such as neurovegetative regulations and endocrine system) involved in this relationship.

After this discussion of some of the constitutional factors thought of importance in determining blood pressure levels, one must look to the environment for a possible explanation of the differences found among the Chinese and Caucasian males. Here we return to our second question at the beginning of this paper, whether differences in diet may account for differences in blood pressure found in the two racial groups. The results seem to indicate a negative answer. Diet was the main and almost only variable in the three Chinese groups who were alike in most other relevant aspects. If diet was a determinant in blood pressure, one would have expected greater differences of the mean blood pressure values among the three Chinese groups, particularly Groups I and III; although it is true that Group I showed the lowest blood pressure values of all the groups at almost all checks, the pressures of Group III were not significantly higher at any time, they were, in fact, lower than the pressures of Group II, which was an intermediate group in regard to diet. One might have expected, also, less differences in mean blood pressure between Groups III and IV whose diet was similar. It can be assumed from the evidence gathered from the weekly food inventory that most of the Chinese students had a similar diet up to the time when they left China, with some regional differences. The change in diet in Groups II and III took place only after their arrival in this country. The average stay in this country was between 4.3 and 5.8 years at the beginning of the study in February to March, 1953. Thus, all one can say at this point is that a change in diet of 4 to 5 years' duration in Group III and a partial change in Group II did not apparently affect the blood pressure levels of these particular individuals. One other factor, possibly of constitutional origin, should be mentioned before concluding this discussion; it is the greater amount of so-called femaleness in the Chinese male, referring mainly to the amount and distribution of body hair. Our findings in this respect support the results of previous investigators.[46-48] Table XVII provides suggestive evidence of a quantitative character that the factor of greater femaleness may actually be a determinant of the blood pressure in the Chinese male: From Table XVII it is evident that the mean pressure in Group IV showed a significantly greater differential between the two sexes than in any of the three Chinese groups throughout all four check periods. In other words, the differential between the pressure levels of the Chinese males and females in our study groups was definitely smaller than in the Caucasian males and females. Males and females in the Chinese groups were less far apart from each other constitutionally and in blood pressure levels than they were in the Caucasians.

SUMMARY AND CONCLUSIONS

A comparative study of 282 Chinese and Caucasian students, from 20 to 45 years of age, of both sexes, in New York City is described. These 282 students

were divided into four study groups with diet as the main variable in the three Chinese groups.

In general, the main differences were found between the three Chinese groups on the one hand and the Caucasian group on the other. Measurements of height, weight, and chest circumference showed significant differences between the two racial groups in both sexes. Historic data on the per cent of cardiovascular-renal diseases in their parents provided evidence for a significantly higher per cent in the Caucasian males. A rough measure of vasomotor instability showed a significantly higher per cent among the Caucasian males and females than in the Chinese.

No correlation was found between height and weight and the lowest blood pressure values.

The following conclusions may be drawn:

1. Mean blood pressure levels in Chinese male students were significantly lower than in Caucasian male students of similar age and socioeconomic status.
2. There were no significant differences in the mean blood pressures of the females in the same groups.
3. Differences in diet did not appear to be of significance in determining differences in mean blood pressures found between the Chinese and Caucasian male students. Before the influence of diet on blood pressure can be considered as insignificant or negligible in our study groups, however, a much longer follow-up would be needed over a period of ten years or more. This is, unfortunately, hardly possible from a practical point of view.
4. Among the constitutional factors examined, differences in height, weight, and chest circumference did not account for the differences in mean blood pressure between the Chinese and Caucasian male students.
5. Significant differences were found in vasomotor instability and the amount of positive family histories of cardiovascular-renal diseases between the two racial groups. To what extent these differences determined the differences in mean blood pressure found between the Chinese and Caucasian male students remained unanswered.
6. Femaleness, a constitutional factor of undiscovered origin, as yet, may play a significant role in determining the lower blood pressures of the Chinese males.
7. Further research is indicated along these lines which should attempt to investigate the endocrine aspects of femaleness with quantitative studies of the various hormones.

SUMMARIO IN INTERLINGUA

Esseva studiate le pression sanguinee de 182 chinese e 100 caucasian studentes a New York. Pro cata subjecto quintuple registrationes esseva facite quatro vices a intervallos de tres menses. In le gruppo chinese le dieta esseva le major factor variabile.

Mesurationes physic, datos de historias familial de morbo cardiovascular, e instabilitate vasomotor monstrava in le caucasianos valores significativemente plus alte. Valores median de pression sanguinee esseva significativemente plus basse in le masculos chinese sed non in le femininas.

Nulle correlation esseva constatate inter pression sanguinee e peso o altor. Le mesurationes physic e le valores median del pression sanguinee differeva minus inter masculos e femininas chinese que inter masculos e femininas caucasian. Isto suggere le possibilitate que le plus grande "femininitate" del masculo chinese es un determinante de su plus basse pression sanguinee.

Differentias in le dieta del chineses non esseva accompaniate per correspondente differentias de pression sanguinee, sed nos debe insister que le signification de iste observationes non pote esser evaluate sin studios multo plus extendite.

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THE ZERO OF POTENTIAL: A PERSISTENT ERROR

H. C. BURGER, D.Sc.

UTRECHT, NETHERLANDS

THE word "potential" is found not only in papers on physics, but also in some papers on medical subjects. This is especially the case in subjects related to the electrical action of the heart, electrocardiography, and vectorcardiography. It might, therefore, be worthwhile to explain from a physical viewpoint an important property of the electrical potential. It must be emphasized that in the following pages it will be supposed that the notion potential, as occurring in medical literature, is the same as the physical one. It is only on this condition that a discussion on this subject between physician and physicist is possible.

Originally the potential is introduced in the theory of electricity as an auxiliary mathematical quantity. It was only after further development of experimental knowledge that it acquired a practical meaning. For a correct understanding it would be necessary to use some mathematics, but this can be avoided by making use of the notion "work". Then we have the definition: The potential difference between the points A and B is equal to the work necessary to bring the unit of positive charge from B to A, or more exactly, it is the quotient of this work for an arbitrary charge and the value of this charge. So work = charge × potential difference.

Such a work function can be calculated from a knowledge of the field along the path of the charge from B to A. If another path is chosen to go from B to A, the work is, according to the law of conservation of energy, the same as in the first case. So the potential difference depends only on the positions of the points A and B. It is this property of the electrical field that gives the thus-defined potential difference its importance.

The work must be computed as a sum of infinitely small contributions over the infinitely small elements of the path; it is an integral. In simple cases, this can be done mathematically and may lead to a simple formula. So if we have a point-shaped fixed charge + q, the field strength is found to be q/r^2 according to Coulomb's law and is directed along the radius r (Fig. 1). Then the result of the calculation is that the potential difference between A and B is:

$$V_A - V_B = q/r_A - q/r_B \qquad (1)$$

From the Department of Medical Physics, Physical Laboratory of the University of Utrecht, Utrecht, Netherlands.

Received for publication Sept. 2, 1954.

But what is the reason that we call this quantity potential *difference* and write it as a difference of two quantities V_A and V_B? This can be seen from Equation (1), if we choose the beginning point B very far away from the charge q, to put it in mathematical terms, in infinity. Then the denominator r_B of the second term at the right side of Equation (1) is very large and the fraction q/r_B, therefore, very small. Then we can neglect q/r_B and find

$$V_A = q/r_A.$$

This is the work that has to be performed per unit of charge to go from infinity to A. It depends only on the position of A in the field.

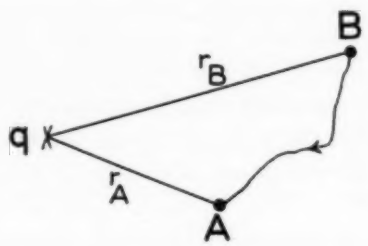

Fig. 1.—The work necessary to bring a unit charge from *B* to *A* depends on the position of the points *B* and *A*. *q* = point-shaped charge.

We see now that the potential difference between A and B can be taken as a difference of two quantities, each depending on the position of one point, A and B, respectively. But it must be borne in mind, that those two quantities V_A and V_B have only a mathematical meaning, and their difference, $V_A - V_B$, is the quantity that matters and can be defined directly, without bringing in infinity.

But the potential difference between two points has indeed the character of a difference. That is to say that if we know the potential difference $V_A - V_B$ between A and a third point C, and know also $V_B - V_C$, then we can find $V_A - V_B$ by subtraction:

$$V_A - V_B = (V_A - V_C) - (V_B - V_C).$$

Therefore, the desire remains to determine the potential of a point itself, without using the unattainable and fictive infinity. Instead of the potential of infinity we want to define a reference potential that has to be the same for all places and all times. The potential of the earth is chosen as such a zero-potential. This is an easy reference point, fulfilling all practical requirements, but it is not at all certain that it is identical with the potential in infinity, as defined mathematically. It is not even certain that the potential is the same all over the earth; it must show differences, indeed, as there are electrical currents inside the earth. But all this does not prevent us from using the earth's potential as a reference point in physics and techniques.

In electrocardiography a lead is a potential difference defined as above. It depends not only on time, but also on the positions of the two electrodes, just as the potential difference $V_A - V_B$ in the preceding simple example. It is not surprising that the question has arisen whether the potentials of each of the electrodes could be recorded. This could be done if there were a reference potential. Infinity cannot be considered practically but the earth can. Now it is certainly possible to record the potential of the left and the right arm for example, separately, with respect to the earth's potential, although this measurement needs some technical refinement to avoid an influence of the connection of the patient to the apparatus on both potentials. But what would be gained by this technique compared with the usual recording of Lead I?

To explain the situation it might be compared to the case of an accumulator. The potential difference between its two poles is 2 volts. This value is determined by the chemical character of the electrodes and of the electrolyte. The chemical reactions inside the accumulator maintain the potential difference of 2 volts, and the reverse, the value of this potential difference gives us some information of these reactions. The knowledge of the potential of either pole with respect to the earth's potential does not add anything to this information. It is determined, not only by the chemistry inside the accumulator, but also by the unessential leakages caused by imperfect insulation against ground. We can influence this situation purposely by connecting the plus pole to ground. It acquires the potential 0, while the other is -2 volts. If the reverse the minus pole is grounded, it has the potential 0 and the plus pole is $+2$ volts. In either case the potential difference is 2 volts. By grounding one pole or the other no information at all is gained as to the processes happening inside the accumulator.

The same is to be found in electrocardiography. We can connect the left or the right arm to ground and get the same electrocardiogram in both cases. It is still the same without any intentional grounding, but in this case the conditions must be such that interference is prohibited. The potential of each electrode with respect to ground could be measured, although with difficulty, but it depends on the uninteresting and accidental leakages of the different points of the body of the patient to grounding. Measurement of both potentials against grounding could not add any information as to the processes inside the patients' body. These processes determine the potential difference in the lead, the potentials themselves (against grounding) depend on the leakages mentioned.

From the preceding it will be clear that the assertion that Wilson's central terminal is on zero potential cannot be correct. The potential difference between all points in the body and on its surface as well as of combined electrodes as the central terminal are determined by the electrical action of the heart. The potential against grounding depends on intentional or accidental ground connections. The central terminal may be connected to ground purposely without influencing any electrocardiogram. If another electrode is grounded, the central terminal gives an electrocardiogram if connected to ground. This can be easily predicted from the extremity leads.

What could then be the meaning of the central terminal? If it is not, that its potential is zero, it could be that its potential is not influenced by the heart

beat. This is often supposed but is not true either. It may be evident from the preceding that we can connect the central terminal to ground, without influencing any electrocardiogram. If it is not grounded purposely its potential with respect to grounding will show a fluctuation. This depends on accidental leakages and is not of any importance.

Perhaps the meaning of the central terminal is only that its potential is the average of the potentials of the extremities so that it is symmetrical with respect to these three. This is not so very important as the extremities themselves are arbitrary electrodes. But this may explain the role played by the central terminal in clinical electrocardiography.

In studying electrical phenomena, we always encounter differences of potential. The differential equation, obtaining for the electrical field, contains differential quotients of the potential, i.e., infinitely small differences; in Ohm's law not the potential itself but a difference of potential occurs. The same is the case in electrochemical phenomena, in cases of piezoelectricity, Stark effect, etc. We may search the literature of physics and chemistry but nowhere do we find a case where it is the potential itself that comes in. We may always add a constant to the potential, and still all laws and formulas hold good. When we sometimes find a formula, in which it looks as if the potential occurs, we always can transform it so that it is written as a relation between potential differences. For this reason a physicist will never try to find the absolute value of a potential or a point of zero potential. He grounds his apparatus, if necessary, at the proper point, without affecting the phenomena he studies.

But it still might be that this general argumentation is not so convincing for a physician as it is for a physicist.

It will be supplemented therefore by a few remarks. The potential V in a point, at a distance r from the dipole M, acting in an infinite homogeneous space, is given by the following formula:

$$V = \frac{M \cos \Theta}{r^2} \quad . \qquad (2)$$

Θ is the angle between the directions of M and r.

This formula for V gives a value zero at infinity, but this is not essential, as we may add a constant C to Equation (2):

$$V = \frac{M \cos \Theta}{r^2} + C \quad . \qquad (2a)$$

This expression obeys the differential equation for V just as well as Expression (2) and describes the observable phenomena in the same way. So the potential of a dipole in infinity is not necessarily zero.

When we enclose the dipole by a conducting envelope, the Formula (2) or more generally Formula (2a) must be changed. This change is relatively significant in the neighborhood of the dipole, but far away from it Expression (2a) must be changed appreciably. At the envelope, V must assume a constant

value, which can be chosen at will. For example it can be zero, i.e., the earth's potential. But the envelope may also have a very high potential. This has, however, no influence whatever on the observable phenomena inside the envelope. These only depend on potential differences, generated by the dipole. This is not only true in this special case of a dipole but holds for all electrical phenomena taking place inside the envelope. Within the large conductors of high voltage generators, human beings can stay without perceiving any effect of the potential, even if this is some million volts above the earth's potential. The electrical effect of their heart beat under these conditions is quite normal, and their electrocardiogram could be recorded without any interference or abnormality.

These circumstances may be compared with those in the gravitational field where there is a potential energy of the bodies analogous to the potential energy (= potential × charge) of an electrical charge in an electric field. If we study the mechanical events of bodies subject to gravitation, e.g., their trajectories, it does not matter if we are at ground level or high up in the mountains. In studying their motion we cannot find the zero level, say the height of the sea level. The latter is an arbitrary zero point, just as the earth's potential. It does not enter essentially in the equations of motion. Here it is only differences of height that matter, just as it is only differences of potential that matter in the electrical phenomena.

From the preceding it may be clear that a so-called unipolar lead has not the simple meaning commonly attributed to it. It cannot be defined as the potential difference of a point of the human body and a point of zero potential, as the latter does not exist. So it can only have a practical meaning. It may be the potential difference between two points, the position of one of which is an essential variable under study, while the position of the other point is always the same. As such, may be chosen Wilson's central terminal, the left leg, or another point which is agreed on.

CONCLUSION

The previously given considerations are of a purely physical nature. They have a bearing on cardiology by the fact that some cardiologists have given their time in trying to find the zero potential. These investigations bear witness to the experimental or theoretical skill of the authors. It is often difficult to find the error in their argumentation, but yet every physicist is convinced that it must be wrong. They spend a good deal of time and interest in their efforts to arrive at a purpose which does not exist. It is superfluous to cite papers here, as it is not the aim of this paper to oppose any authors but to warn seriously all cardiologists interested in potential problems not to waste their time that they can spend so much better. Should there yet be a real problem in looking for a practically predilected reference potential, then this problem must be solved in collaboration with those who have had the schooling and training to treat it in the proper way.

SUMMARY

Any point of an inanimate system or of a human body can be connected to earth to obtain zero potential. The processes inside the system are independent of this connection. It is only the potential differences which matter. An absolute value of the potential does not enter in the physical laws and, therefore, can never be determined. An essential zero-potential does not exist.

SUMMARIO E CONCLUSIONES IN INTERLINGUA

Omne puncto del corpore human —exactemente como omne puncto de non importa qual systema inanimate —pote esser connectite al terra con le resultato de un potential zero. Le processos intra le systema es independente de iste connexion. Lo que importa es exclusivemente le differentia del potential. Un valor absolute del potential non figura in le leges del physica e per consequente non pote esser determinate. Il existe nulle potential zero essential. Nonobstante, certe cardiologos se ha effortiate a trovar lo. Le objectivo de iste articulo es prevenir omne cardiologos que illes non deberea guastar lor tempore in tal vanitates. Investigationes de iste typo non contribuera unquam a nostre cognoscentias del processos electric que es generage per le activitate del corde.

THE ACTIVATION OF THE FREE LEFT VENTRICULAR WALL IN THE DOG'S HEART

In Normal Conditions and in Left Bundle Branch Block

Demetrio Sodi-Pallares, M.D., Abdo Bisteni, M.D., Gustavo A. Medrano, M.D., and Fernando Cisneros, M.D.

Mexico City, Mexico

During the last decade there have appeared in the medical literature numerous papers[1-17] concerning the ventricular activation in normal and pathologic conditions. Some of the newer findings are in disagreement with the classical concepts of Lewis and Rothschild.[18,19] Many of these recent findings must be more critically analyzed before acceptance. We will attempt to point out various factors which may introduce errors.

1. *The Use of Direct-Writing Machines as a Recording Method.*—Obviously, this type of recording is unsatisfactory for experimental purposes, especially when we are dealing with conduction rates of thousands of millimeters per second. Some of our experiments can not escape this criticism. Undoubtedly, Einthoven's string galvanometer used by Lewis is a better means of recording than the modern direct inscription.

2. *Unipolar Lead Recording.*—The intrinsic deflection in this type of lead corresponds, approximately, to the arrival of the activation crest at the exploring electrode.[2] Often the inscription time of this deflection takes more than 0.01 sec. Therefore, it is important to know which part of the intrinsic deflection corresponds to the abrupt diminution of membrane impedance in the muscle fibers which are in contact with the exploring electrode. Some authors have chosen the vertex of the intrinsic deflection as that moment, i.e., when the explored region is still a source of current. We believe this is not the best moment, and this can be proved by means of close bipolar simultaneous leads.[2,17] In the unipolar lead we have considered the nadir of the intrinsic deflection as a better reference point for determining the moment of arrival of the activation crest.[2,17] However, close simultaneous bipolar leads show that any point along the deflection may correspond to the vertex of a continuous bipolar lead.[2,17] These results indicate that unipolar recording is not the most satisfactory method for the study of the arrival of the stimulus at a certain region. Lewis' work cannot escape this criticism.

From the Department of Electrocardiography of the Instituto Nacional de Cardiología de México.
Received for publication Sept. 3, 1954.

3. *The Degree of Injury Produced by the Exploring Electrodes in the Unipolar and/or Bipolar Leads.*—The injury current produces important changes in the morphology of the unipolar tracing: the R wave increases in voltage, the S wave tends to disappear or may do so, and the intrinsic deflection is delayed.[20] Not even these changes could be considered constant since they vary with time. The injury diminishes as time elapses. The majority of authors have paid little or no attention to the importance of this fact. Therefore, the presence of an RS-T displacement in a unipolar tracing qualifies the curve as unsatisfactory. If no RS-T shift is observed, the morphology of the QRS complex may be accepted as satisfactory. A small amount of injured tissue has little influence upon the contiguous bipolar recording and the intrinsic phenomenon is practically unmodified. Once again we wish to emphasize that the best method of determining the moment of arrival of the activation crest is through the use of bipolar leads.

4. *Unsatisfactory Contiguous Bipolar Leads.*—Recently, several investigators have illustrated their publications with contiguous bipolar tracings whose duration and form are unsatisfactory. The bipolar lead may be considered satisfactory when the intrinsic phenomenon has a duration under 0.01 sec. We have observed that if the intrinsic phenomenon lasts less than 0.01 sec. the main deflection remains unmodified even though the stimulus travels by different pathways, for instance, the activation of sinus origin and heterotopic impulses. The total duration of a close bipolar tracing is generally shorter than that of the unipolar one. Hence, a close bipolar tracing whose form and duration resemble those of a simultaneous unipolar curve should be excluded. In some contiguous bipolar tracings no main deflection can be seen. Instead, the curve shows an intrinsic phenomenon of great rapidity, which permits its recognition. We believe that it is better to record simultaneously the unipolar and bipolar tracings. If this is done, it will be possible in the majority of cases to make the experiments more accurate.

ILLUSTRATIVE MATERIAL

We feel that the most satisfactory tracings have been published by Durrer.[13,14]

Recently, we have had the opportunity to use a double-beam cathode-ray oscillograph.* With this type of recording our unipolar and bipolar tracings are more satisfactory. The characteristics of the cathode-ray tube, type 322, can be found in the Dumont catalog. We have also used three amplifiers of Grass, model P4A†. The curves obtained with the cathode-ray tube were photographed with the Kymographic Camera Grass, model C-4-C.

The close bipolar leads shown in Fig. 1 are very satisfactory, particularly the lower one. The duration of the main deflection in the upper tracing is less than 0.01 sec. The intrinsic deflection of the lower bipolar tracing is inscribed as a line.

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*This apparatus was generously donated to our Department by Mr. George H. Bryant of Los Angeles, Calif.

†These amplifiers and the camera were donated to us by the Rockefeller Foundation.

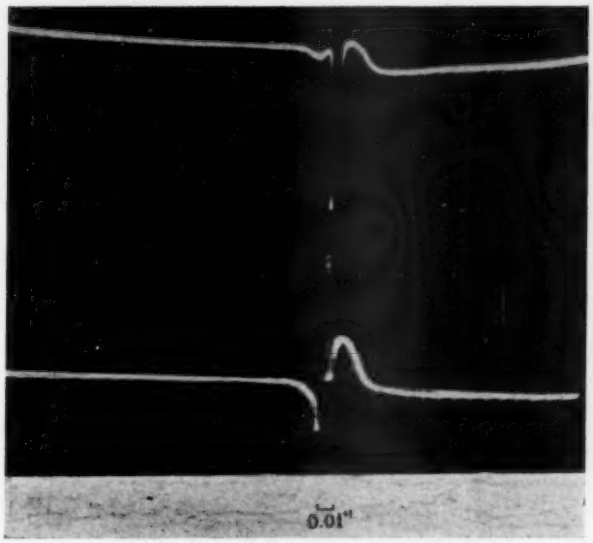


Fig. 1.—Close bipolar tracings. The duration of the intrinsic deflection of the lower bipolar tracing is less than 0.01 sec. The upper bipolar was obtained at the endocardial surface of the free left ventricular wall; the lower bipolar at 2 mm. from the other pair of electrodes, i.e., in the mass of the free left ventricular wall.

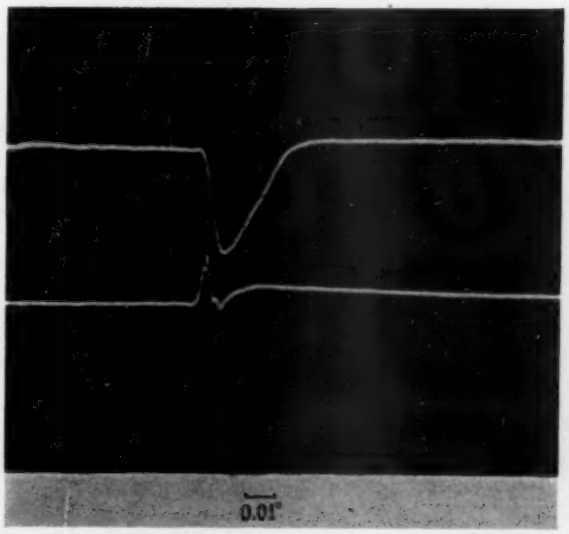


Fig. 2.—The upper tracing is unipolar and was obtained simultaneously with a close bipolar record. The exploring electrode of the unipolar lead was at the same time one of the electrodes of the close bipolar lead. Notice the difference in duration of both tracings. The vertex of the bipolar is simultaneously inscribed with some point of the intrinsic deflection in the unipolar.

The upper tracing of Fig. 2 is unipolar and was registered simultaneously with a close bipolar lead. We consider the bipolar lead as satisfactory because the duration of the main deflection is less than 0.01 sec. The vertex of the bipolar lead, which we believe represents the arrival of the activation at the area being explored, is simultaneously inscribed with some point of the intrinsic deflection of the unipolar lead but not with its beginning nor with its ending. In other words, if the vertex or nadir of the intrinsic deflection in the unipolar curve be chosen as the moment in which the stimulus reaches the exploring electrode, then this selection will be incorrect and the result erroneous.

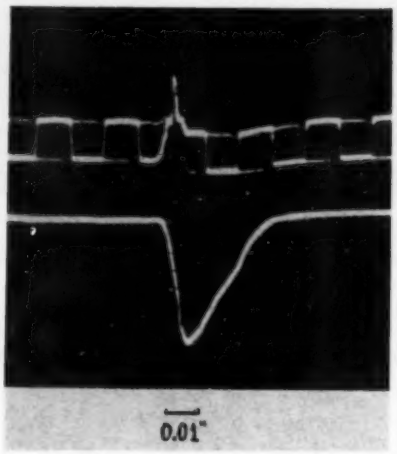


Fig. 3.—The upper tracing is a close bipolar and the main deflection lasts around 0.002 sec. The lower tracing is unipolar and was obtained with one electrode of the bipolar record (see text for discussion).

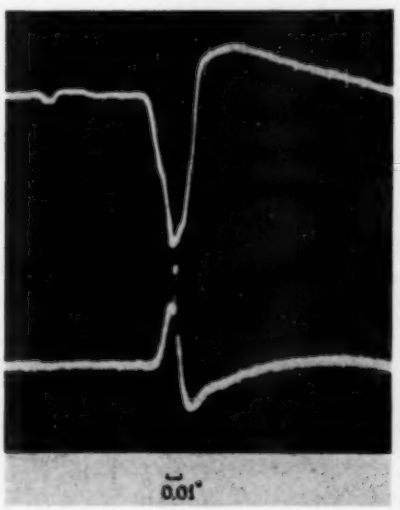


Fig. 4.

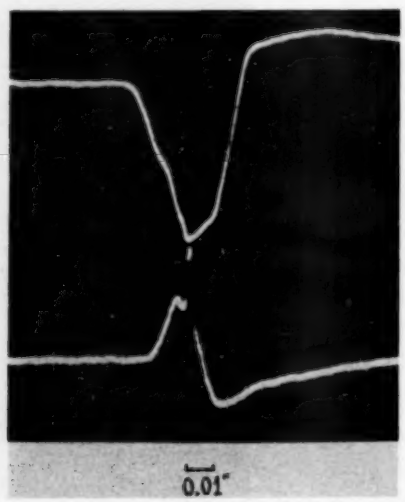


Fig. 5.

Fig. 4.—A bipolar tracing (lower curve) registered simultaneously with a unipolar from the same site. The intrinsic phenomenon of the bipolar is inscribed as a line and does not correspond to the intrinsic deflection of the unipolar.

Fig. 5.—The same tracings as in Fig. 4 taken at higher speed.

The bipolar tracing in Fig. 3 is a good example because the main deflection lasts around 0.002 sec. The correctness of this figure can be better appreciated if the duration of the intrinsic phenomenon in the bipolar is compared with the duration of the squares produced by the alternating current (in Mexico City the frequency of the alternating current is 50 cycles per sec.).

In Fig. 4, the bipolar tracing is also satisfactory, and it is registered simultaneously with a unipolar lead from the same site. The intrinsic phenomenon of the bipolar lead (lower tracing) is inscribed as a line and does not correspond to the intrinsic deflection of the unipolar lead. Fig. 5 shows the same tracings as Fig. 4 taken at higher speed.

The tracings of Fig. 6 were obtained with a direct-writing apparatus. The lower curve is the best bipolar tracing we have been able to register with this type of machine. The vertex of the main deflection in the bipolar lead corresponds to the final portion of the intrinsic deflection of the unipolar leads (superior and middle curves) obtained with the same electrodes of the bipolar tracing.

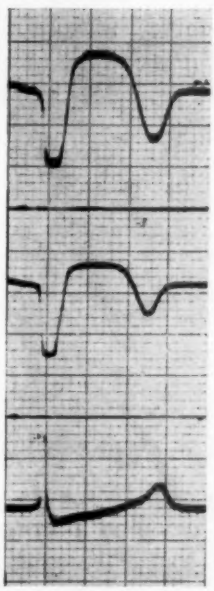


Fig. 6.—Tracings obtained with a direct-writing apparatus. The lowest tracing is a close bipolar, and its vertex corresponds to the final portion of the intrinsic deflection of the unipolar leads (upper and middle curves) obtained with the same electrodes of the bipolar tracings.

In Fig. 7 two contiguous bipolar leads are shown. These were obtained from the free wall of the left ventricle. The lower tracing is the same bipolar shown in Figs. 4 and 5. The upper tracing is of great duration and almost all the curve corresponds to extrinsic phenomena; nevertheless, a rapid deflection is inscribed near the second vertex. This is an example of a technically defective bipolar curve with which it is still possible to determine the moment of electrical activation between the two electrodes. In order to make sure that this rapid line actually corresponds to the intrinsic phenomenon, we registered the same bipolar

tracing, at a higher speed, with the unipolar curve obtained from one of the bipolar electrodes (Fig. 8). The rapid line of the bipolar was inscribed at the same time as the inferior point of the intrinsic deflection in the unipolar.

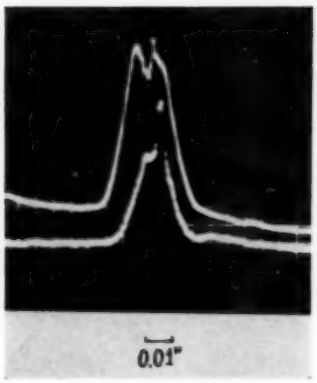


Fig. 7.

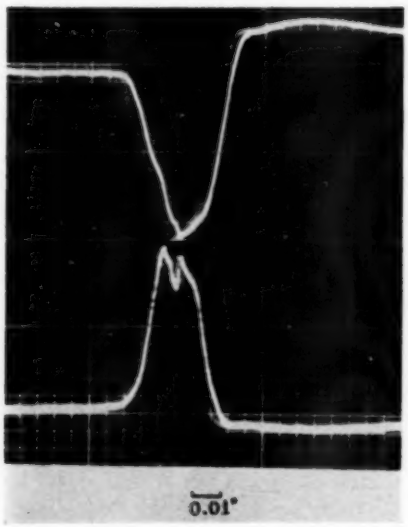


Fig. 8.

Fig. 7.—Contiguous bipolar tracings obtained from the free wall of the left ventricle. The upper curve is not a satisfactory one; nevertheless, the intrinsic phenomenon is recognized (see text).

Fig. 8.—The lower tracing is the same bipolar as that of the upper curve shown in Fig. 7 and it was taken at higher speed simultaneously with the unipolar tracing (upper curves) obtained from one of the bipolar electrodes (See text).

NORMAL ACTIVATION PROCESS IN THE FREE WALL OF THE LEFT VENTRICLE

In general, the findings reported by Lewis and Rothschild[18,19] for the free ventricular walls continue to be accepted as correct: (a) the activation process develops from the endocardium to the epicardium; (b) the mean direction of activation is from the apex to the base. Nevertheless, against Lewis' supposition, we have found, as have other authors, important variations in the conduction rate of the nonspecific muscle fibers of the free ventricular walls.

Durrer[21] and Rodríguez and associates[6] presented papers at the Inter-American Congress in Buenos Aires, Argentina, affirming that the conduction rate in the muscular portions of the wall proximal to the endocardium reaches much higher values than those given by Lewis. Figures of 2,000 mm. per sec. or higher are common and occasionally these subendocardial muscle masses are activated simultaneously with others of the same ventricular wall located several millimeters from the endocardium. It is to be noted that Rodriguez and collaborators (in our department) used the direct-writing apparatus, and thus the same criticism of their results can be offered as was mentioned in the first paragraph of this paper.

Because of this, we have recently repeated these measurements using the cathode-ray oscillograph. The close bipolar tracings showed an intrinsic phenomenon of very small duration and the determination of the speed of the activation wave was relatively simple.

The results were similar to those described by Durrer and Rodríguez. In at least one-half of the muscle mass proximal to the endocardium, the conduction rate was 2,000 mm. per sec. or more. The bipolar tracings were often simultaneous in the endocardium and in muscular portions located several millimeters from the endocardium (about 5 or 6 mm.). In a very few cases an intramural area, several millimeters distant from the endocardium, was activated before an endocardial area located at the same level, giving the impression that the stimulus approached the endocardium instead of moving away from it.

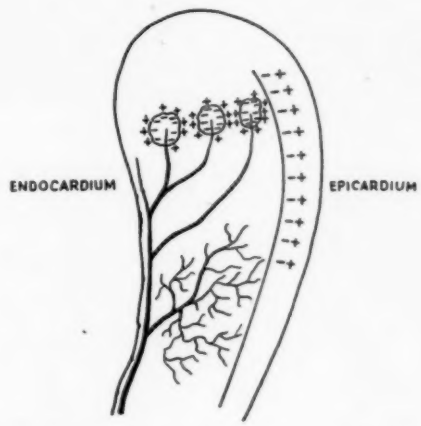


Fig. 9.—Schematic representation of the activation process in the inner portions of the left ventricular wall. Multiple simultaneous islands of negativity appeared when the electrical impulse arrived at these regions (see text). As the impulse reaches the outer third of the free wall, the conduction rate is reduced and an electrical double layer is formed with the positive poles oriented toward the epicardium.

In a few cases the speed figures are inferior to 2,000 mm. per sec.; we have found values of 800, 900, 1,200 and 1,600 mm. per sec. Even though there is a great variation, we must stress that in the majority of cases, the values were over 2,000 mm. per sec.

Recently, Prinzmetal and his collaborators[9] described in these areas the morphology of the unipolar tracings. They found QS complexes in two-thirds of the thickness of the free left ventricular wall in those regions most proximal to the endocardium. Our unipolar tracings, obtained with the cathode-ray tube, show the same morphology, that is, there is no initial positivity, the tracings are only negative, of the QS type, as Prinzmetal and his collaborators described.

Recently, Cabrera and Sodi-Pallares[22] explained why the activation of those regions proximal to the endocardium is not registered in the proximal and distant unipolar tracings. Contrary to that which is to be expected, the impulse does not give rise to positive deflections in the direct unipolar tracings obtained from

that muscle mass. Furthermore, if the subendocardial mass is the seat of a healed infarct, the subepicardial unipolar leads taken at this level will have a normal morphology.[9] Thus, one would imagine that the epicardial unipolar tracing is due to the activity of the subepicardial tissue and that the contribution of the subendocardial mass is negligible. In order to explain this phenomenon we can

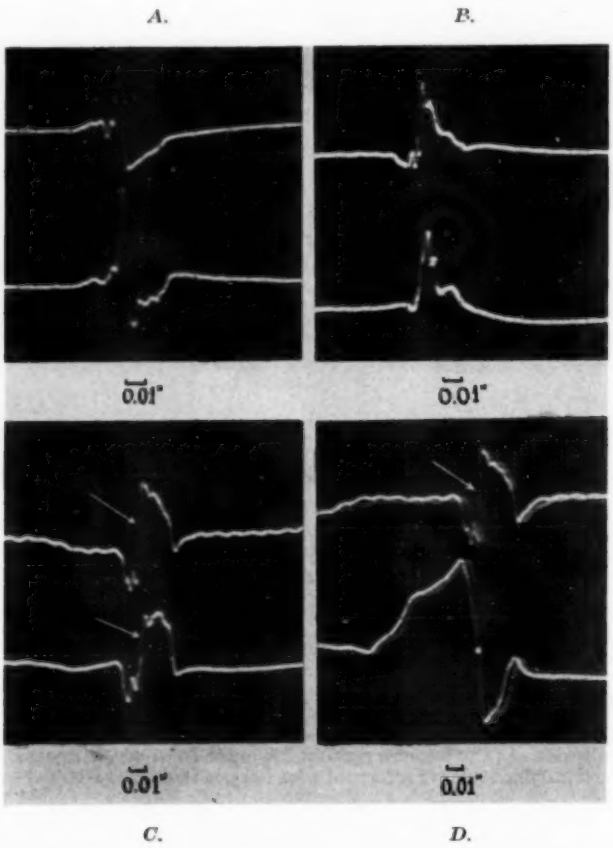


Fig. 10.—Contiguous bipolar tracings: *A*, control; *B*, incomplete left bundle branch block; *C*, complete left bundle branch block. In *D* one of the bipolar curves was simultaneously recorded with its corresponding unipolar.

imagine the existence of multiple simultaneous islands of negativity when the electrical impulse arrives at these regions. These islands of negativity would form closed regions of polarization (Fig. 9) and the vectorial forces would be neutralized. This conclusion has as a mathematical basis the theorem of Gauss. A similar suggestion regarding the activation of the endocardial surfaces was made by Einthoven[23] as early as 1908.

If the above is considered as correct, then, we may imagine that after such simultaneous activity the electrical impulse would pass from the subendocardial to the subepicardial mass. The conduction rate would be reduced as the impulse reaches nonspecific pathways; and at this moment there would be an electrical double layer (Fig. 9) with the positive poles oriented toward the epicardium.

Consequently, we believe that the major part of the muscle mass of the left ventricular wall would lack electrocardiographic expression in the unipolar tracings. Nevertheless, the total electrical effect in the free walls is as if the wave of activation, conceived as a double layer, travels from the endocardial to the epicardial surface.

In Fig. 10,*A*, are shown two contiguous bipolar tracings obtained within the free wall of the left ventricle. A pair of electrodes (upper tracing in Fig. 10,*A*) was located at 4.5 mm. from the endocardium; another pair (lower tracing in Fig. 10,*A*) was placed 6.5 mm. from the same endocardial surface. The two sites were explored at the same level with the Mandoki type electrodes which have been described.[3] Since the curves were satisfactory, they were registered at higher speed (Fig. 11) in order to simplify the measurement of conduction rate between the two areas explored. The result was 1,560 mm. per sec., that is, a higher figure than that usually assigned to the nonspecific fibers of the heart.

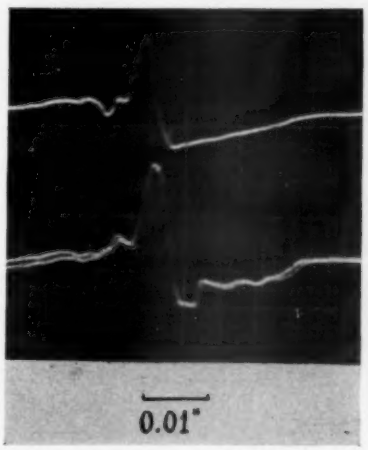


Fig. 11.—The same tracings as in Fig. 10,*A* taken at higher speed.

In Fig. 12,*A*, the unipolar tracings obtained from the same areas are shown. They are of the QS type, that is, there is no initial positivity at 6.5 mm. from the endocardium in a ventricular wall with a total thickness of 9 mm.

The conduction rate diminishes in the areas proximal to the epicardium; thus, Rodríguez and collaborators[8] found that in the muscle fibers subjacent to the epicardium of the left ventricle, the speed of the activation wave reaches average values of 300, 290, 200, and in some cases 500 mm. per sec. In the right ventricle the muscle fibers subjacent to the epicardium demonstrated conduction rates of a higher magnitude than those of the left ventricle, and it was possible to obtain values of 900 and 1,000 mm. per sec.

In Fig. 13, two contiguous bipolar tracings are shown; the upper was obtained at 2.5 mm. from the epicardium and the lower at 3.8 mm. from the same surface. The corresponding electrodes were placed at the same level in the free wall of the left ventricle. The conduction rate calculated for this interelectrodal distance was 265 mm. per sec.

ACTIVATION OF THE FREE LEFT VENTRICULAR WALL IN LEFT BUNDLE BRANCH BLOCK

There are various authors[15] who consider that the activation of the free left ventricular wall is not only delayed when a left bundle branch block is present but that other important changes also appear in the sequence and in the pathways followed by such a process. Our results with direct-writing apparatus show that the various grades of bundle branch block do not modify the sequence, direction, or the conduction rate in the free ventricular walls. With the cathode-ray oscillograph we repeated these experiments in order to be sure of the results.

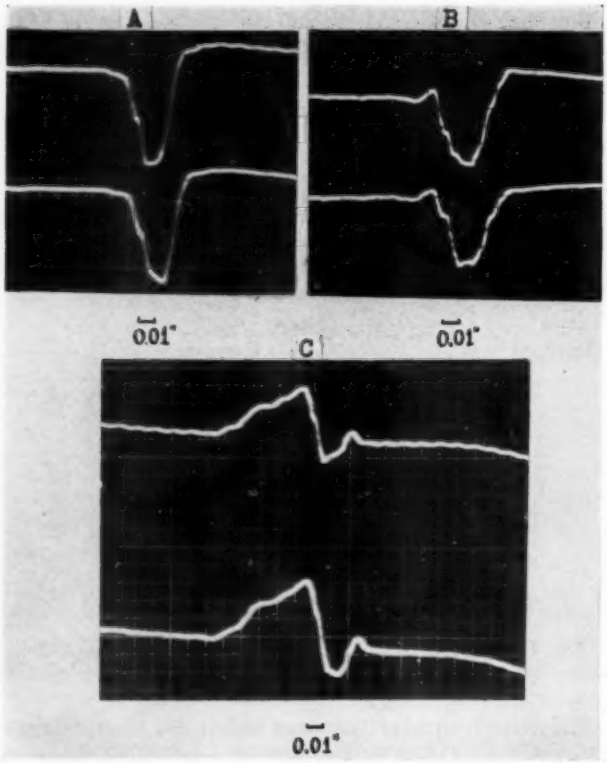


Fig. 12.—Unipolar tracings: *A*, control; *B*, incomplete left bundle branch block; *C*, complete left bundle branch block (see text).

It is necessary to be sure that the points being explored are thoroughly removed from the interventricular septum. Actually the interventricular septum extends to both sides of the anterior and posterior longitudinal sulcus and the investigator may erroneously believe that he is exploring the free ventricular wall when in reality he is exploring the septum. This occurs mainly in the recording of epicardial tracings. On the other hand, we must not forget that there are muscular portions which are activated by the right bundle branch and which are situated to the left of the anterior descending artery. The activation of the interventricular septum in the presence of bundle branch block is very complex and will not be analyzed in this paper.

We have shown that the tracings of Fig. 12,*A* are unipolar and correspond to two sites of the free left ventricular wall. The upper tracing is intramural and was obtained 4.5 mm. from the endocardium; the simultaneous unipolar lead, lower tracing, (Fig. 12,*A*) was registered 6.5 mm. from the endocardium. The morphology of the intrinsic deflection in both tracings is very similar. In the lower tracing the intrinsic line is inscribed 0.0033 sec. later than that of the upper tracing. In Fig. 12,*B* the same tracings are shown with incomplete left bundle branch block. The intrinsic deflections present the same morphology and the registration time which separates them is the same as that in the tracings without bundle branch block. The unipolar tracings of Fig. 12,*C* were obtained in the same sites and correspond to complete left bundle branch block. Again the intrinsic deflections are very similar and again the separation time is of 0.0033 sec. It does appear, then, that the activation time has not been modified in this interelectrodal zone.

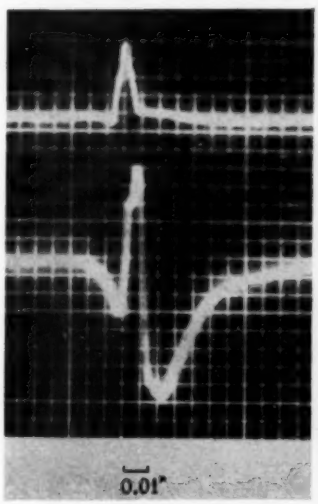


Fig. 13.

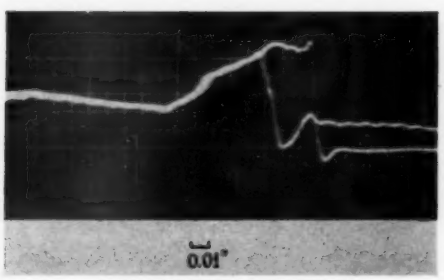


Fig. 14.

Fig. 13.—Contiguous bipolar tracings. The upper was obtained at 2.5 mm. from the epicardium, and the lower at 3.8 mm. from the same surface.

Fig. 14.—Unipolar epicardial and endocardial tracings obtained at the same level of the free left ventricular wall after complete left bundle branch block was produced. The tracings are superimposed in order to better appreciate the differences in time of activation and in morphology.

In order to eliminate any doubt which may arise through the use of unipolar leads, bipolar registrations were obtained in the same areas and with the same grades of bundle branch block. We have already mentioned that Fig. 10,*A* shows contiguous bipolar tracings and the vertices of the main deflections are separated by 0.003 sec. which is a similar value to that shown by the unipolar leads in Fig. 12. This figure remains the same with incomplete bundle branch block (Fig. 10,*B*). The contiguous bipolar tracings which are shown in Fig. 10,*C* were obtained in the same sites when there was complete left bundle branch block. There are many important extrinsic phenomenon in these bipolar leads;

however, two rapid deflections (marked by arrows) can be easily identified and we consider them as representative of the muscular activation between the two electrodes of each bipolar lead. The separation between these deflections of rapid inscription is again 0.003 sec. One of the bipolar leads, when the block was complete, was registered simultaneously with its corresponding unipolar lead (Fig. 10,*D*) and the line which we have considered as intrinsic in the bipolar is simultaneous with the white point shown on the intrinsic deflection of the unipolar lead.

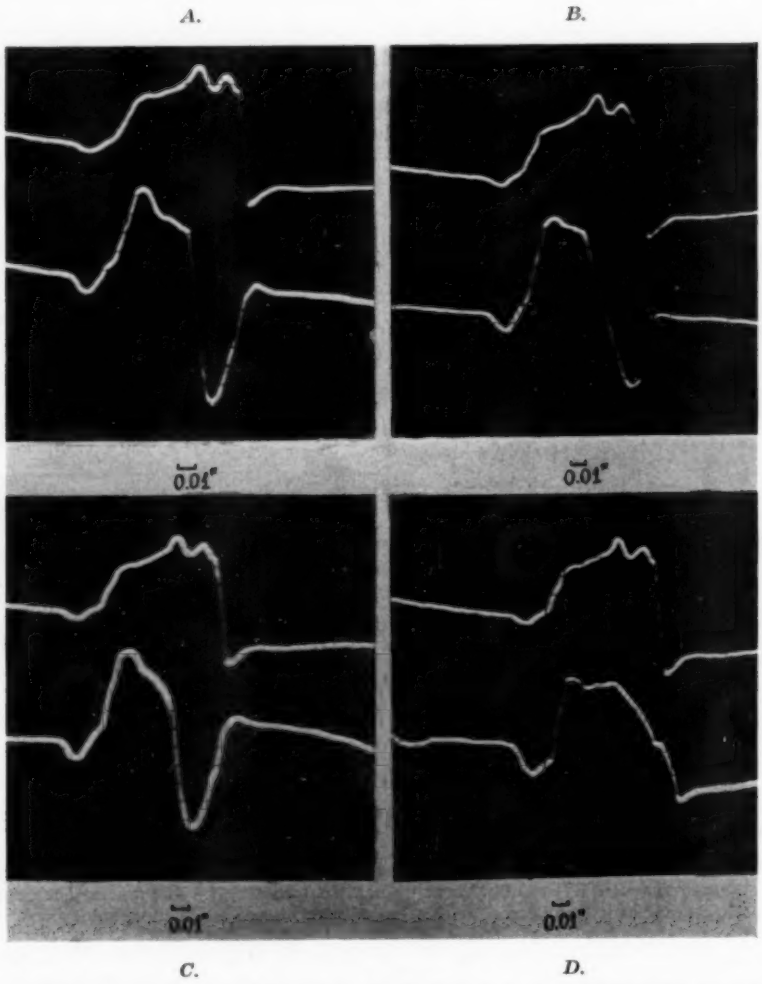


Fig. 15.—The upper tracings of each section (*A*, *B*, *C* and *D*) correspond to the same unipolar lead obtained on the epicardial surface of the left ventricular wall in the presence of left bundle branch block. The lower tracing in *A* is an intracavitary unipolar registered close to the left ventricular apex. The lower tracing in *B* was obtained close to the center of the left ventricular cavity. The lower unipolars in *C* and *D* were obtained high in the left ventricular cavity.

This is just one example of many experiments which have been carried out in a similar manner using the direct-writing apparatus. The activation of the free wall is not modified in its direction nor in its sequence with the various grades of left bundle branch block.

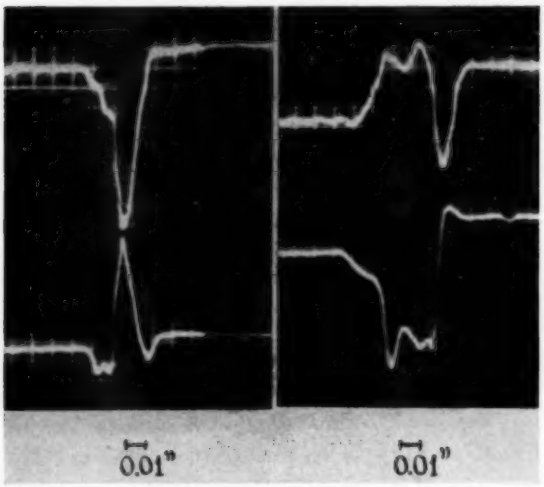
In the same experiment we registered, simultaneously, the unipolar endocardial and epicardial tracings at the same level of the free left ventricular wall (Fig. 14). As can be seen in this figure the tracings were superimposed in order to appreciate better the differences in time and in morphology. The upstroke of the R wave in the superimposed endocardial tracing coincides exactly with the major part of the upstroke of the R wave in the epicardial tracing. This exact super-position of the positive waves shows a common origin which we believe is due to the activation of the interventricular septum. When the intrinsic deflection of the endocardial tracing is inscribed the epicardial curve still remains above the isoelectric line which is due to the activation of the muscular mass of the free left ventricular wall. The thickness of the wall at this level was 9 mm. The middle points of the intrinsic deflections in both tracings are inscribed with a time difference of 0.023 sec. The calculated conduction rate was 391 mm. per sec.

Recently, Kennamer and Prinzmetal described the potential variations in the left ventricular cavity in left bundle branch block and found that in some cases the intraventricular tracing is only positive. It should be pointed out that the intracavitary potential variations are not alike at different levels of the cavity and that important morphologic variations can be found if the exploring electrode is placed close to the apex or near the base.

The upper tracings of each section (*A*, *B*, *C*, and *D*) of Fig. 15 correspond to the same unipolar tracing obtained after left bundle branch block on the epicardial surface of the free left ventricular wall, at a site half way between the base and the apex. The lower tracing in *A* is an intracavity unipolar registered close to the left ventricular apex; it shows a qRS morphology. The lower tracing in *B* is also an intracavitary unipolar and was obtained close to the center of the cavity, and in comparison with the former its S wave is of less magnitude. The lower tracing shown in *C* was obtained in the upper portion of the left ventricular cavity and is, in general, similar to that shown in *B*. The tracing in *D* was taken in the high posterior portion of the left ventricular cavity. The Q is similar to those of the other intracavitary curves and the S wave has practically disappeared. In order to register these different curves we used a completely insulated needle with the exception of its terminal tip. Special care was taken to keep this terminal tip away from the ventricular septum and from the endocardium of the free ventricular wall.

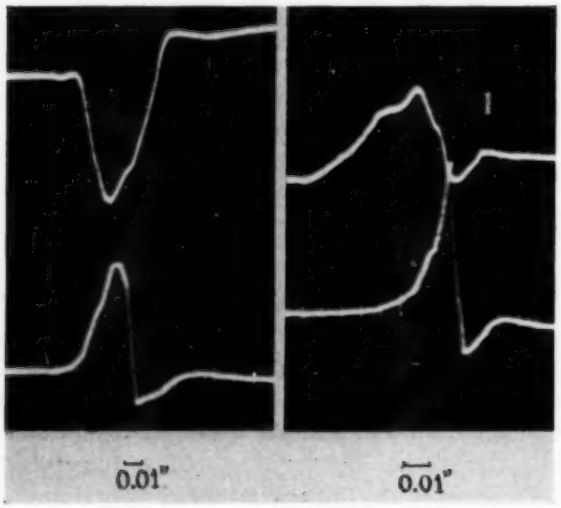
We have not registered intracavitary tracings as those shown by Kennamer and collaborators. We admit that the unipolar tracings may be strictly positive in some areas close to the interventricular septum, but in the tracings that we obtained, the morphology showed definite notching or slurring of the QRS complex contrasting with the smooth curves obtained by the aforementioned authors. We feel that the differences in the curves obtained were due to the use of different recording apparatus. The direct-writing machine obviously may show great inertia as compared to the cathode-ray tube. This brings to mind some curves of injury or artifacts obtained with high inertia apparatus.

When there is complete left bundle branch block the free left ventricular wall activation is delayed, but the sequence and sense of the activation process are not modified. The electrical septal forces acquire considerable importance



A. *B.*

Fig. 16.—The tracings in *A* are control, and in *B* after complete left bundle branch block. The upper curves were obtained in the left ventricular cavity. The lower tracings are distant bipolar with one electrode on the right septal surface and the other on the left septal surface.



A. *B.*

Fig. 17.—The tracings in *A* are control and in *B* after complete left bundle branch block. The upper curves were obtained in the left ventricular cavity. The lower tracings are distant bipolar with one electrode on the endocardial surface and the other on the epicardial surface of the free left ventricular wall.

in the determination of curve morphology. To understand this it is sufficient to remember that the intracavitary tracings may be completely positive. In addition, a bipolar tracing with one electrode on the right septal surface and another on the left septal surface (Fig. 16) shows the important magnitude of those septal vectors.

The electrical forces of the free left ventricular wall are the same in left bundle branch block as in the controls, but they may be masked by the septal vectors (Fig. 17).

Summarizing, we may say that our results are in disagreement with the opinions and findings of other investigators. We believe that these differences are due to the following facts:

1. Results obtained through the exclusive use of unipolar lead.
2. Erroneous interpretations of these tracings. This occurs when one considers that they only register the electrical phenomenon from small areas of the heart, when in reality the diffuse character of these leads is well established.
3. The selection on these curves of a constant fixed point on the intrinsic deflection as representative of the moment of arrival of the stimulus at the exploring electrode. The errors which may arise from such a practice are many.
4. Erroneous exploration of septal regions instead of the free left ventricular wall.
5. Failure to take into account a current of injury produced by the pressure of the exploring electrodes.
6. The use of nonsatisfactory bipolar leads.
7. Interpretation of incomplete bundle branch block as complete bundle branch block. We must not forget that, frequently, the grade of bundle branch block diminishes during the experiment.

SUMMARY

In this study a critical attempt was made to review some of the more recent experimental studies on ventricular activation.

A study of the activation of the normal free ventricular wall using the cathode-ray tube confirmed our previous observations. The spread of activation in the subendocardial muscle mass and at least one-half of the thickness of the adjacent free ventricular wall, reaches values of 2,000 or more mm. per sec. In these regions QS complexes are recorded as described by Prinzmetal and collaborators. An attempt to explain this morphology is presented.

In left bundle branch block the sequence, sense, and speed of activation in the free left ventricular wall are unchanged as compared to the normal control. The alterations in morphology are mainly due to changes in direction of activation and delay of conduction in the interventricular septum.

SUMMARIO IN INTERLINGUA

Iste studio representa un tentativa a revider critic amente alicunes del plus recente investigationes experimental in re le activation ventricular.

Un studio del activation del libere e normal pariete ventricular per medio del tubo a radios cathodic confimava nostre previe observationes: Le propagation del activation in le massa muscular subendocardiac e al minus in un medietate del spissitate del adjacente libere pariete ventricular attinge valores

de 2.000 e plus mm/sec. In iste regiones complexos QS es registrate de accordo con le description de Prinzmetal e su collaboratores. Nos ha tentate explicar iste morphologia.

In bloco de branca sinistre le sequentia, le direction, e le velocitate del activation in le libere sinistre pariete ventricular exhibi nulle cambiamentos in comparison con illos de controlos normal. Le alterationes morphologic esprincipalmente debite a cambiamentos de direction del activation e a un retardo de conduction in le septo interventricular.

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A NEW TECHNIQUE FOR THE REGISTRATION OF THE VECTORCARDIOGRAM BASED ON THE MATHEMATICAL RELATION BETWEEN THE LIMB AND PRECORDIAL LEADS

CARLOS AYALA Y DE LANDERO

GUADALAJARA, MEXICO

MANY methods to obtain vectorcardiograms have been proposed; all of them have been based on the theoretical assumption of the thorax as a geometrical imaginary figure. It is obvious that the thorax can not be accepted as an unvariable geometrical figure.

Therefore, the best system is not the determination of a figure similar to that of the thorax, but the supposition of three axes perpendicular to each other determining no special figure. These axes are vertical, horizontal, and sagittal, all of them passing through the center of the myocardic activation.

A method to obtain an approximate vectorcardiogram in the frontal and horizontal planes was proposed in a foregoing communication.[1] There was not a common lead for both planes, and they were obtained separately.

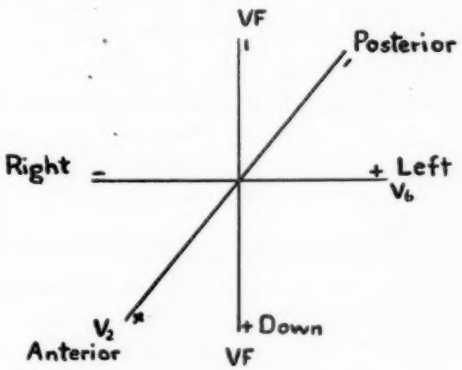

Fig. 1.

PROPOSED METHOD

As one can see in Fig. 1, precordial leads V_2 and V_6 and unipolar limb lead VF form a triaxial system fulfilling approximately the aforementioned conditions. These leads may be considered practically perpendicular to each other, and the three planes are formed as seen in Fig. 2. However, unipolar extremity lead VF is registered at a larger distance than that of the precordial leads. Therefore, these leads must be corrected to have a valid mathematical relation between them.

From the Gabinete de Cardiología y Nefrología del Hospital Civil de Guadalajara, México. Facultad de Medicina de la Universidad de Guadalajara, México.

Received for publication Sept. 20, 1954.

By accepting the validity of Einthoven's triangle, unipolar limb Lead VF is registered at the same distance as Lead VL. This lead has a simple relation with precordial lead V_6 as one can see in Fig. 3. Therefore, the obtention of a formula giving a relation between the limb and precordial leads is facilitated (Fig. 3).

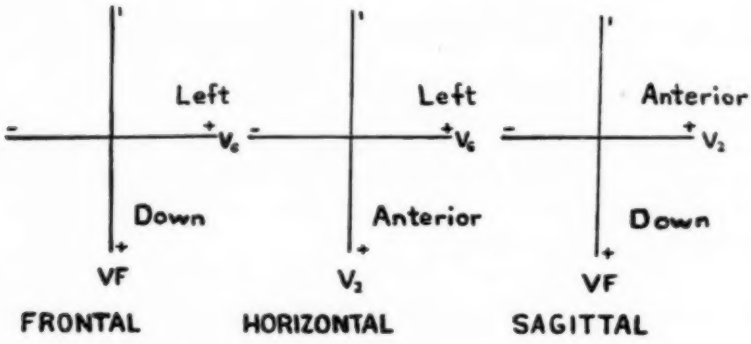

Fig. 2.

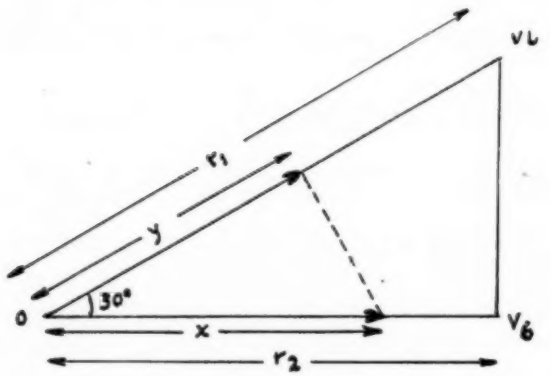

Fig. 3.

$$VP = \frac{\cos X}{r^2}$$

$$V_6 = x = \frac{\cos 0^\circ}{r_2^2} = \frac{1}{r_2^2}; \quad VL = y = \frac{\cos 30^\circ}{r_1^2} = \frac{0.8660}{r_1^2}$$

$$r_2 = 0.8660\, r_1; \quad r_2^2 = 0.7499\, r_1^2; \quad r_1^2 = \frac{0.8660}{y}$$

$$x = \frac{1}{0.7499\, r_1^2} \quad \therefore \quad x = \frac{1}{0.7499 \dfrac{0.8660}{y}} = \frac{y}{0.6394}$$

Therefore:

$y = 0.6394\ x; \quad x = 1.5640\ y$

As one can see in the foregoing formulas, the limb leads must be augmented 1.5640 to be combined with precordial leads. With the same purpose precordial leads may be diminished 0.6394.

Both procedures are valid; however, it is easier to augment the limb leads. The augmented unipolar extremity leads are approximately registered in the same conditions. Therefore, augmented limb lead aV_F may be utilized, and the results will be obtained almost exactly.

The obtention of an approximate vectorcardiogram in the frontal and sagittal planes from the electrocardiogram may be done with the help of formulas and tables suggested for the horizontal plane in a previous communication.[1]

SUMMARY AND CONCLUSIONS

A method for the registration of the vectorcardiogram is proposed. This method consists in the assumption of a triaxial system formed by precordial Leads V_2 and V_6 and limb Lead VF as perpendicular to each other.

A formula to correct and to obtain a mathematical relation between precordial and limb leads is given. The correction of the limb Lead VF is approximately the same as that obtained with the technique for the registration of augmented unipolar limb Lead aV_F. The use of this lead results in direct application to the method and also in simplification.

No special technique for the registration of the vectorcardiogram is suggested, and results may be compared simply with the electrocardiogram, in which the same leads suggested here are commonly used.

SUMMARIO IN INTERLINGUA

Es proponite pro le registration de vectocardiogrammas un methodo non basate super le representation del thorace per un geometric figura theoric sed super le postulato que le derivationes precordial V_2 e V_6 forma insimul con le derivation de extremitate VP un systema triaxial rectangular. Es disveloppate un formula que permitte le adjustamento del derivationes V_2, V_6, e VP al relation mathematic mentionate.

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THE DETERMINATION OF INDIVIDUAL ENLARGEMENT OF THE VENTRICLES BY RADIOLOGIC METHODS

Based Upon Autopsy and Angiocardiographic Findings in the Left Anterior Oblique Position

Jorge Ceballos, M.D.,* Roberto Calderon, M.D.,** and Otto Kargl, M.D.***

Galveston, Texas

THE difficulty in evaluation of ventricular enlargement by fluoroscopy or routine films is well known and has been emphasized in a previous paper.[1] Consequently, the method based upon measurement of the heart shadow in the left anterior oblique position has been used, and by this means more precise measurements are possible.

Studies by Fray[2] on autopsy cases and O'Kane and associates[3] on clinical cases and our angiocardiographic studies in left anterior oblique position have shown the interventricular septum to be in the center of the cardiac silhouette except in its inferior portion. In this lowest segment, the septum makes a small curve downward and posteriorly to reach the well-known shallow identation which indicates the ending of the interventricular septum. By this line, the heart is divided into two parts; the anterior half is formed by the right ventricle and the posterior half corresponds to the left ventricle.

Following the interventricular septum line upward as described above it will show that it extends precisely to the posterior contour of the ascending aorta. On the bases of these features, we have the necessary data for finding the interventricular septum, either fluoroscopically or on the films in the left anterior oblique position. At fluoroscopy it will be sufficient to turn the patient enough to visualize the margins of the aorta. The posterior margin of the aorta cannot always be identified on the radiograms. In that event we have to measure first the aortic diameter in the posteroanterior view using the method described by Kreuzfuchs[4] from the barium-filled esophagus or the air-filled trachea to the outer border of the aortic knob. We may then locate the posterior border of the aorta on the left anterior oblique view by measuring its diameter from the anterior portion, which is always visible as it emerges from the anterior contour

Received for publication Sept. 12, 1954.

*Roentgenologist, Instituto Nacional de Cardiologia, Mexico D. F. (on leave); at present, Assistant Professor of Radiology, The University of Texas, Medical Branch, Galveston, Texas.

**Ex-Assistant Professor of Radiology, The University of Texas, Medical Branch; at present, Radiologist at Managua, Nicaragua.

***Ex-Resident, Dept. of Radiology, The University of Texas, Medical Branch: at present, Radiologist, University of Innsbruck, Austria.

of the cardiac shadow in this projection. The interventricular septum will correspond to a line which follows the heart axis and goes from the posterior margin of the aorta to the inferior portion of the heart shadow just above the small curve which will reach the well-known shallow identation representing the inferior portion of the septum. Once we have localized the septum, we trace two perpendicular lines to extend to the cardiac shadow in its most convex part. The anterior one will represent the width of the right ventricle, mostly the in-flow tract according to Nemet and Schwedel,[5] and the posterior that of the left ventricle (Figs. 1-4).

The present paper is a study of this method and a review of the findings in one hundred and fifteen cases which have been checked with the clinical diagnosis, electrocardiography, and in some instances with angiocardiography, surgery, or at autopsy.

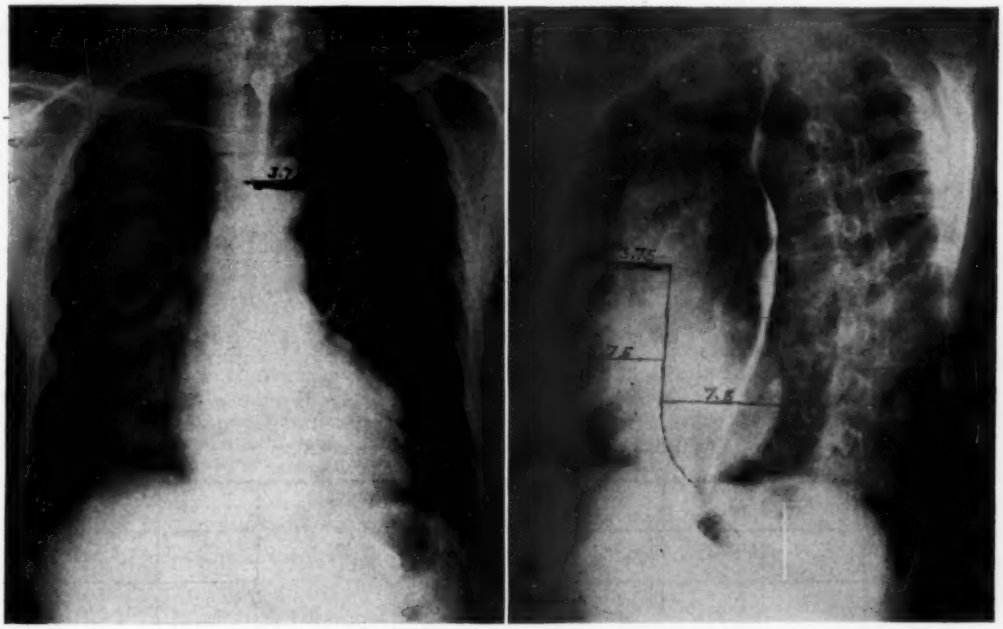


Fig. 1.—Posteroanterior and left anterior oblique views. B. E., 63-year-old white male with chief complaint of shortness of breath. B. P., 175/90. E. C. G., Q-T upper limits of normal; left-axis deviation. Left ventricular hypertrophy. Incomplete left bundle branch block. Myocardial abnormality anterolaterally. Diagnosis: hypertensive heart disease.

Table I gives a general idea of the types of cases used in this study.

Tables II and III and Fig. 1 record the data in the hypertensive cases. The number of cases is too small to be taken in consideration for statistical purposes, yet our findings agree with the general knowledge of left ventricle changes in

TABLE I

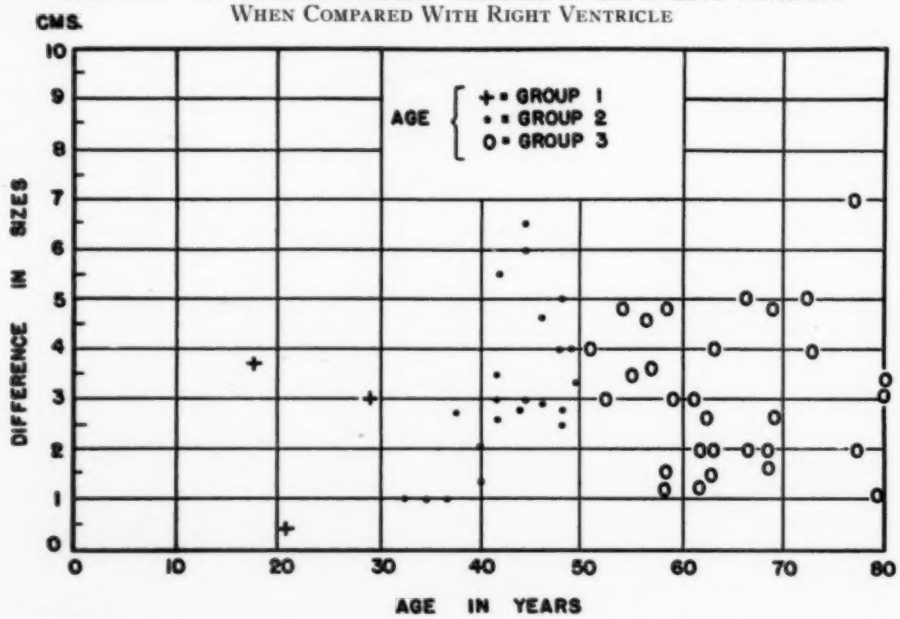
DISEASE	RADIOLOGIC FINDINGS CONCERNING THE VENTRICLES	NO. OF CASES
Hypertensive heart disease	Predominance of enlargement of the left ventricle	55
Syphilitic aortic regurgitation	Enlargement of the left ventricle	15
Arteriosclerosis	None or slight enlargement of left ventricle	5
Mitral valve disease	None or predominance of the enlargement of the right ventricle	35
Total		110
Anemia	Moderate globular enlargement of the heart	2
Heart in pregnancy	Slight globular enlargement of the heart	3
Total		5

TABLE II. HYPERTENSIVE HEART DISEASE (55 CASES)

NO. OF CASES	RACE AND SEX				AGE GROUP (YEARS)	SIZE AVERAGE (CM.)		
	W.F.	N.F.	W.M.	N.M.		AORTA	LEFT VENT.	RIGHT VENT.
3	2	1	0	0	Group 1 0 to 30	2.40 to 3.00	4.80 to 9.00	4.50 to 7.00
22	2	7	8	5	Group 2 31 to 50	2.50 to 5.90	6.00 to 13.00	3.75 to 7.00
30	4	7	7	12	Group 3 51 or more	2.70 to 5.20	6.00 to 13.00	4.20 to 9.50

W. F. = white female; N. F. = Negro female; W. M. = white male; N. M. = Negro male.

TABLE III. HYPERTENSIVE HEART. INCREASE IN SIZE OF LEFT VENTRICLE WHEN COMPARED WITH RIGHT VENTRICLE



hypertensive heart disease. (A) Most of the patients were more than 30 years of age. (B) There were more Negroes than Caucasians, more males than females. (C) As it was previously reported,[1] in no case were the left and right ventricular measurements the same. The difference in size between the right and left measurements increased with the number of cases studied, and this was always more than 1.5 cm.

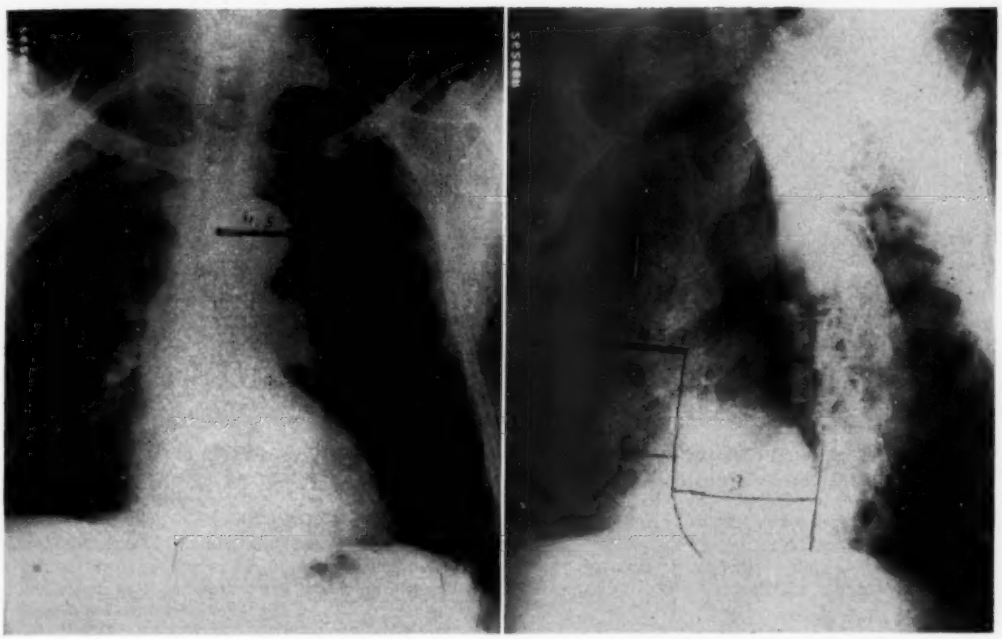


Fig. 2.—Posteroanterior and left anterior oblique views. J. W., 69-year-old Negro male with chief complaint of pain on left side of chest. Dyspnea on exertion. B. P., 172/108. Diastolic shock felt in aortic area. Aortic systolic rumbling murmur and aortic diastolic murmur. Kahn positive. E. C. G., left-axis deviation, semihorizontal electrical position. Left ventricular hypertrophy. Multifocal ventricular prematures. Diagnosis: syphilitic aortic regurgitation.

Tables IV and V and Fig. 2 summarize the findings in the cases of syphilitic aortic regurgitation. Our findings in these cases were very similar to those in our hypertensive cases.

TABLE IV. SYPHILITIC AORTIC REGURGITATION (15 CASES)

NO. OF CASES	RACE AND SEX				AGE GROUP (YEARS)	SIZE AVERAGE (CM.)		
	W.F.	N.F.	W.M.	N.M.		AORTA	LEFT VENT.	RIGHT VENT.
2		1		1	GROUP 1 0 to 30	2.50 to 2.75	6 to 8.20	4.50 to 5
5		2		3	Group 2 31 to 50	3.10 to 4	6 to 11	4.75 to 9
7	1	1		5	Group 3 51 or more	3.5 to 5	7.5 to 11.50	4.50 to 7

W. F. = white female; N. F. = Negro female; W. M. = white male; N. M. = Negro male.

TABLE V. SYPHILITIC AORTIC REGURGITATION INCREASE IN SIZE OF THE LEFT VENTRICLE WHEN COMPARED WITH THE RIGHT VENTRICLE

NO. OF CASES	DIFFERENCE IN THE SIZE OF VENTRICLES (CM.)
0	None or in favor of the right ventricle
1	0 to 0.50
1	0.50 to 1.00
3	1.00 to 2.00
3	2.00 to 3.00
7	More than 3.00

Tables VI and VII, arteriosclerotic cases, were made up mostly of patients 50 years old or more, and there was only a minimal enlargement of the left ventricle.

TABLE VI. ARTERIOSCLEROSIS (5 CASES)

NO. OF CASES	RACE AND SEX				AGE GROUP (YEARS)	SIZE AVERAGE (CM.)		
	W.F.	N.F.	W.M.	N.M.		AORTA	LEFT VENT.	RIGHT VENT.
0					Group 1 0 to 30			
1		1			Group 2 31 to 50	3.30	6.20	6.90
4	1	1	1	1	Group 3 51 or more	3.00 to 4.50	6.20 to 7.50	5.50 to 7.00

TABLE VII. INCREASE IN SIZE OF LEFT VENTRICLE WHEN COMPARED WITH RIGHT VENTRICLE

NO. OF CASES	DIFFERENCE IN SIZE OF VENTRICLES (CM.)
1	None or in favor of right ventricle
2	0 to 0.50
2	0.51 to 1.00
0	More than 1.00

Tables VIII and IX and Figs. 3 and 4 showed findings which were opposed to the previous cases; the predominant chamber enlarged was the right ventricle.

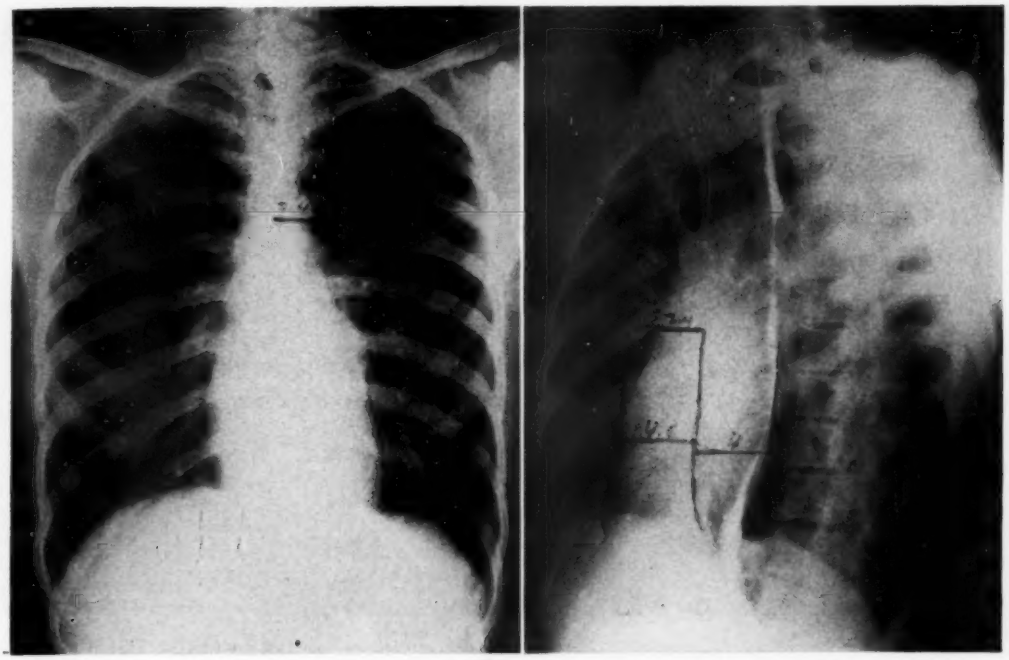


Fig. 3.—Posteroanterior and left anterior oblique. C. M. L., 26-year-old white female. Rheumatic fever when 6 years of age; progressive shortness of breath on exertion and orthopnea. B. P., 120/70. No palpable thrill, no enlargement to percussion. Loud hard Grade 3 harsh blowing systolic murmur from mitral area and to apex and axilla. Diastolic murmur over mitral area. E. C. G., right-axis deviation, left atrial abnormality. Minor S-T depressions which could be due to digitalis. Diagnosis: mitral lesion, predominance of mitral stenosis. Surgical procedure: The mitral orifice was palpated with the finger tip, the opening was about the size of a kitchen match. Dilatation with the finger, no commissurotomy.

TABLE VIII. MITRAL HEART (35 CASES)

NO. OF CASES	RACE AND SEX				AGE GROUP (YEARS)	SIZE AVERAGE (CM.)		
	W.F.	N.F.	W.M.	N.M.		AORTA	LEFT VENT.	RIGHT VENT.
21	6	8	7		No. 1 0 to 30	1.5 to 3.5	4 to 7.5	4 to 8.5
13	6	2	2	3	No. 2 31 to 50	2.5 to 3.5	4.7 to 8.5	5.3 to 9
1				1	No. 3 51 or more	3.75	6	5

W. F. = white female; N. F. = Negro female; W. M. = white male; N. M. = Negro male.

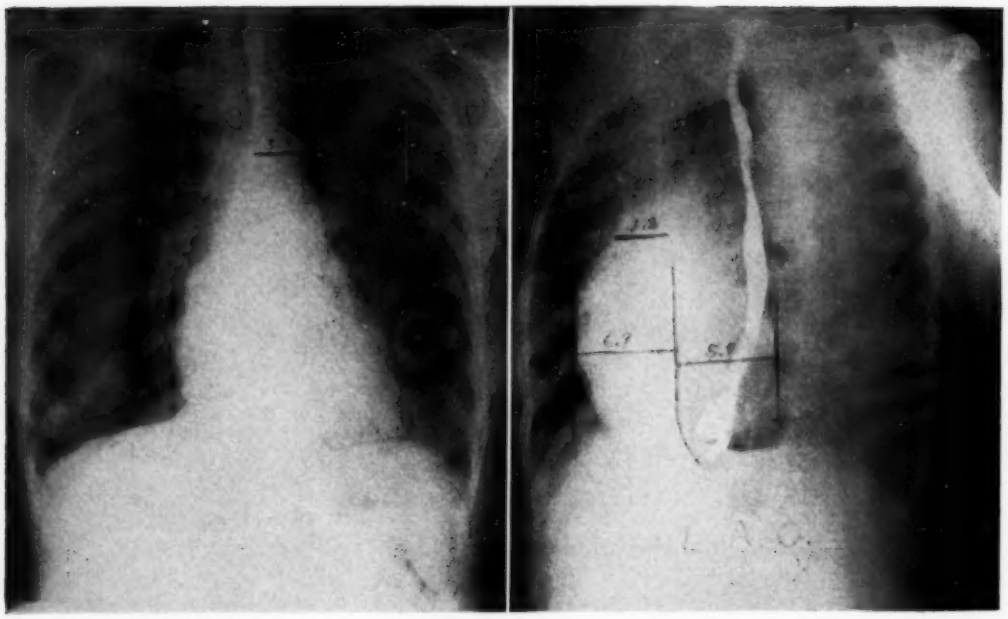
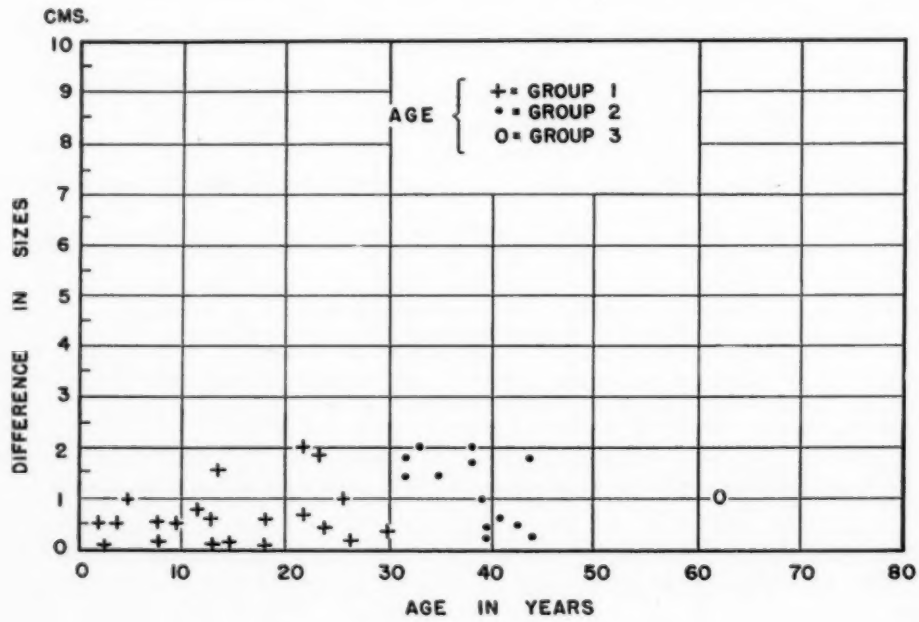


Fig. 4.—Posteroanterior and left anterior oblique views. W. K., 45-year-old Negro female. Shortness of breath on exertion. B. P., 130/90. No thrills. Heart enlarged to percussion. Soft apical systolic murmur, mid-diastolic murmur at apex. E. C. G., right-axis deviation. Anterolateral subendocardial ischemia. Rapid auricular fibrillation. Angiocardiography: left atrium enlarged, delay in emptying through mitral valve. Diagnosis: mitral lesion, predominance of mitral stenosis. Patient rejected surgical treatment.

TABLE IX. MITRAL HEART. INCREASE IN SIZE OF RIGHT VENTRICLE WHEN COMPARED WITH LEFT VENTRICLE



There is, however, less tendency to differences than there was in the cases of predominant left ventricular enlargement. This is, of course, the result of the mitral configuration of the heart in which, if the stenosis is predominant over the insufficiency, it shows enlargement of the right ventricle. On the other hand, if the lesion is "double mitral" there will be enlargement of both ventricles.

In the two cases of anemia and three of normal pregnancy, there was a moderate globular enlargement of the heart contour which is the usual finding.

SUMMARY

A follow-up of a method for individual measurement of the ventricles is presented. It is based upon the localization of the interventricular septum in the left anterior oblique position. One hundred and fifteen additional cases were used. The results previously described show again the value of the method.

SUMMARIO IN INTERLINGUA

Le objectivo de iste studio, que es basate super 115 casos, es demonstrar le valor de nostre methodo pro determinar le allargamento individual del ventriculos per medios radiologic in le position oblique sinistro-anterior (O. S. A.) del thorace. Le methodo se basa primarimente super le constatation angiocardiographic que in le perspectiva O. S. A. le septo interventricular es in le centro del silhouette cardiac e divide lo per consequente in duo portiones. Le portion anterior corresponde al ventriculo dextere, le portion posterior al ventriculo sinistre. Ambe ventriculos es normalmente equidimensional in le position O. S. A. In casos de predominante allargamento sinistro-ventricular—como per exemplo in morbo cardiac hypertensive e in insufficientia aortic—nos constatava que le portion posterior esseva plus grande que le anterior. In casos de morbo mitral le portion anterior esseva plus grande que le posterior.

Iste methodo es usabile in fluoroscopia e radiophotographia. Illo es plus utile in fluoroscopia.

We wish to gratefully acknowledge the assistance received from Dr. George Herrmann in editing this article.

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A STUDY OF ELECTROCARDIOGRAMS RECORDED DURING EXERCISE TESTS ON SUBJECTS IN THE FASTING STATE AND AFTER THE INGESTION OF A HEAVY MEAL*

CLAYTON H. KLAKEG, M.D., RAYMOND D. PRUITT, M.D., AND HOWARD B. BURCHELL, M.D.

ROCHESTER, MINN.

THE object of this study was to compare the changes induced in the electrocardiogram by exercise in human subjects in the fasting state with the changes induced in these same persons after they had ingested a large meal. Seventy-six subjects were included in the study. Most of them had experienced pain in the chest, the origins of which commonly were not clear on the grounds of clinical evidence available prior to the test.

PROCEDURE

The exercise accomplished by the subjects in the course of a test consisted of forty ascents and descents of two steps, each step being 9 inches high. However, exercise was terminated at any time during the test if the subject complained of fatigue, dyspnea, or of discomfort in his chest. No subject was given the test if, on the basis of his clinical record, it was evident that the procedure was more strenuous than were those activities in which he engaged each day. No subject was tested who had developed pain in relation to exertion during the weeks immediately preceding his clinical examination. Excluded also were those whose tolerance for exercise was decreasing progressively during that period immediately prior to their clinical examination.

Electrocardiograms consisting of Leads I, II, III, aV_R, aV_L, aV_F, V_1, V_3, and V_5 were recorded just before the subject exercised, immediately after he exercised, and 5 minutes after he exercised. If any changes had occurred in the electrocardiogram immediately after exercise, then tracings were taken also after 2 minutes and 8 minutes of rest. If changes persisted longer than 8 minutes, then additional electrocardiograms were obtained at later intervals, until such time as the pattern returned to its configuration before exercise.

Repetition of the test after the ingestion of a large meal was accomplished within a period of 24 hours following the test performed when the subject was

From the Mayo Clinic and Mayo Foundation.
Received for publication Sept. 21, 1954.

*Abridgement of thesis submitted by Dr. Klakeg to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine.

in a fasting state. The postprandial test was carried out within the hour following the meal, whereas the fasting or routine test was done two or more hours after the subject had ingested any food. The subject of the test was encouraged to eat what he considered to be a large meal.

Some words of explanation should be offered regarding the manner in which subjects of the test were placed in the two categories, "coronary disease" and "no heart disease." The majority of the subjects included in this study and all of those classed as having "coronary disease" were patients. In many, the routine exercise test was requested by the clinician because he desired the information afforded by the results of the test as a diagnostic aid. Since the results of the test sometimes were equivocal and since a negative result did not exclude the possibility of coronary disease in the patient, obviously not all diagnostic problems which came to the laboratory were resolved therein. By what means and by what justification, then, does a division of subjects into two categories, one with and one without heart disease, come about?

In answering the question, reference must be made to those assumptions under which the study was instituted. These were (1) that the uses and limitations of the exercise test as a diagnostic aid had been well defined by the experience of other investigators and by work in our own laboratory and (2) that the criteria for a positive result with the exercise test were defined to our own satisfaction in our own laboratory (see COMMENT). The object of this study was not to strive specifically for further knowledge pertaining to these assumptions. Rather, the object was to determine whether an exercise test carried out after a heavy meal had certain clinical applications which would render it a useful diagnostic technique. The conclusion was reached that evidence bearing on this answer would be acquired in a form most readily comprehended if an extensive system of diagnostic categories was avoided. Hence, all clinical evidence including the results of the test was used in placing subjects of the test in one or the other of the two diagnostic categories. When doubt persisted as to the diagnosis even with all evidence at hand, the subject arbitrarily was placed in that category which seemed the most likely if not the established one.

Let it be recognized that, by such a method, the presentation of our data has been distorted in a measure. For example, in Fig. 4, the amount of shift in the RS-T segment during the exercise test is greater in subjects of the category "coronary disease" than in those classed as having no heart disease. But some of the subjects in the category "coronary disease" were placed there because deviations in the RS-T segment developed during the exercise test, and perhaps some subjects with coronary disease were improperly classed as being without it, because the results of the exercise test were negative.

These considerations do not bear significantly, in our judgment, upon a comparison of the results of an exercise test carried out before and after a heavy meal.

RESULTS

Of the seventy-six subjects, sixty-four were men and twelve were women. They were divided into groups according to age (Fig. 1) and the majority were in the 40 to 59 year group. The age range was for the total group 19 to 62 years,

for the men 26 to 61 years and for the women 19 to 62 years. The average age for the entire group was 46.4 years, for the men 46.5 years and for the women 45.8 years. Of the sixty-four men undergoing the test, twenty-six were placed in the category designated "coronary disease" and thirty-eight in the category "no heart disease"; of the twelve women, seven were placed in the first and five in the second of the two groups.

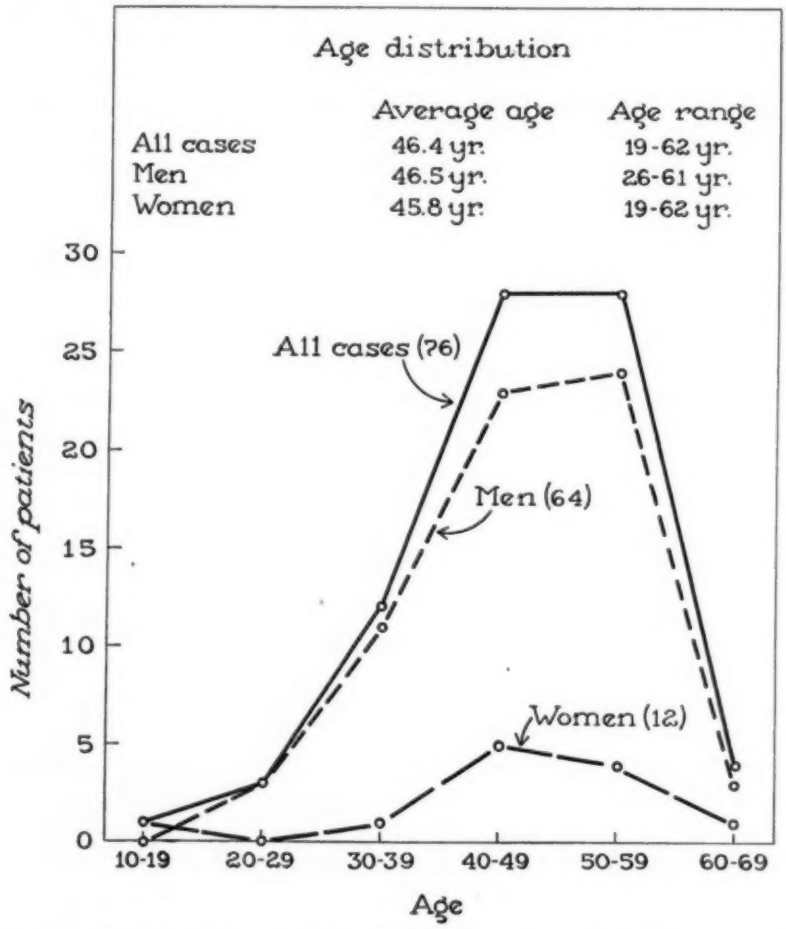


Fig. 1.—Age-distribution curves with the average age and the age range for the men, women, and total subjects.

The large majority of the group were normotensive. The range in systolic blood pressure was from 100 to 180 mm. Hg. The weight of the subjects varied from 110 to 246 pounds.

In the routine exercise tests the average cardiac rate was 78.6 at rest, 101.2 immediately after exercise, and 82.6 after 5 minutes of rest. In tests performed after a heavy meal the average cardiac rate was 86.4 at rest, 112.6 immediately after exercise, and 91.3 after 5 minutes of rest (Fig. 2).

The Q-T interval fell within the normal range (Fig. 3).

The mean of the levels of the RS-T segments relative to the levels of the P-R segments in Lead V_5 (Fig. 4) was determined from "resting, control" elec-

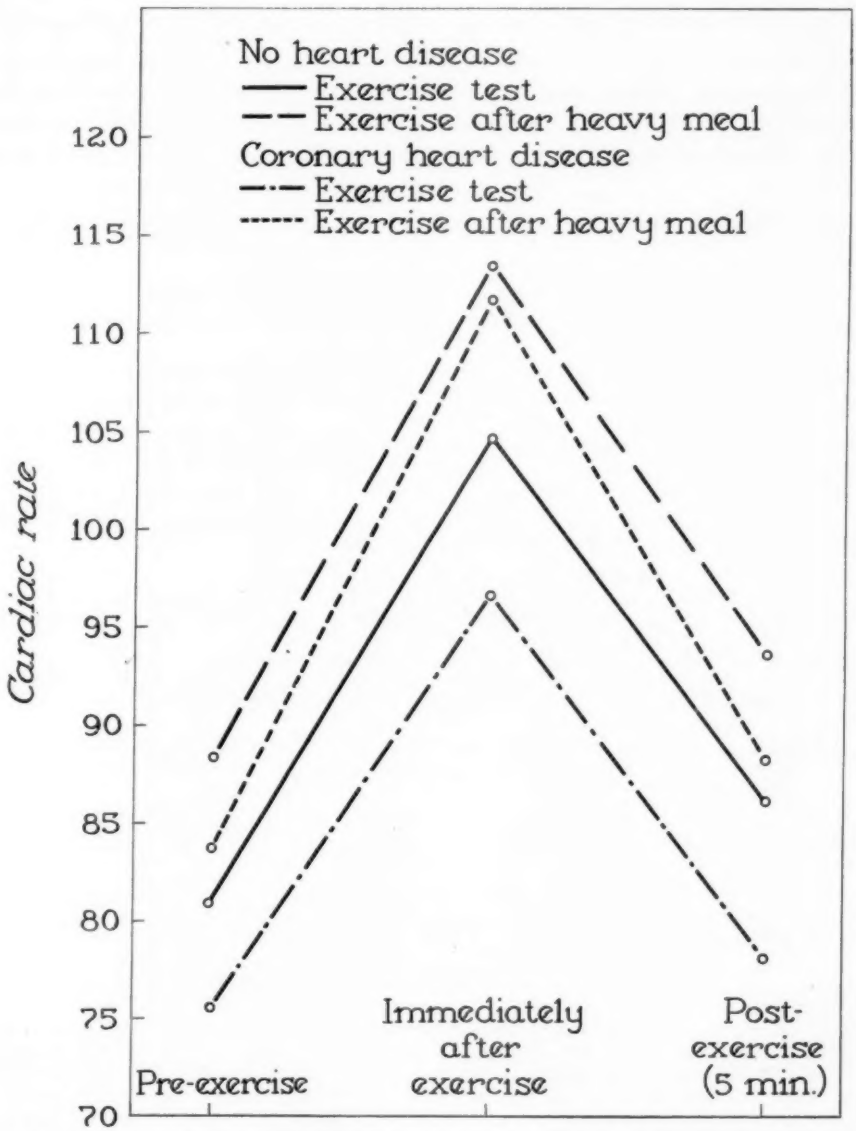


Fig. 2.—Cardiac rates during various phases of the exercise test and of the exercise test performed after a heavy meal.

trocardiograms of all patients in the series and found to be +0.18 mm. Following the routine exercise test, the mean of all levels of the RS-T segments in this same lead was −0.36 mm. For the entire group of subjects in the tests done after a heavy meal, the figure for the mean in the "resting, control" records was +0.06 mm., whereas following exercise it was −0.55 mm.

Similar calculations were carried out for that group of subjects to whom a final clinical diagnosis of coronary disease was attached, and for a group whose members finally were considered as free of evidence of heart disease. In the "coronary disease" group, the mean of the levels of RS-T segments in the "resting, control" electrocardiograms was +0.14 mm., and this mean dropped to −0.71 in the records made immediately after exercise. When the members of this same group were tested after a heavy meal, the initial value of the mean was −0.05 mm. and following exercise the value was −0.98 mm. In the group labeled "no heart disease," these values in the routine test were +0.20 for the "resting, control" tracings and −0.09 for the postexercise records. In the test performed after a heavy meal, the values were +0.16 and −0.20, respectively.

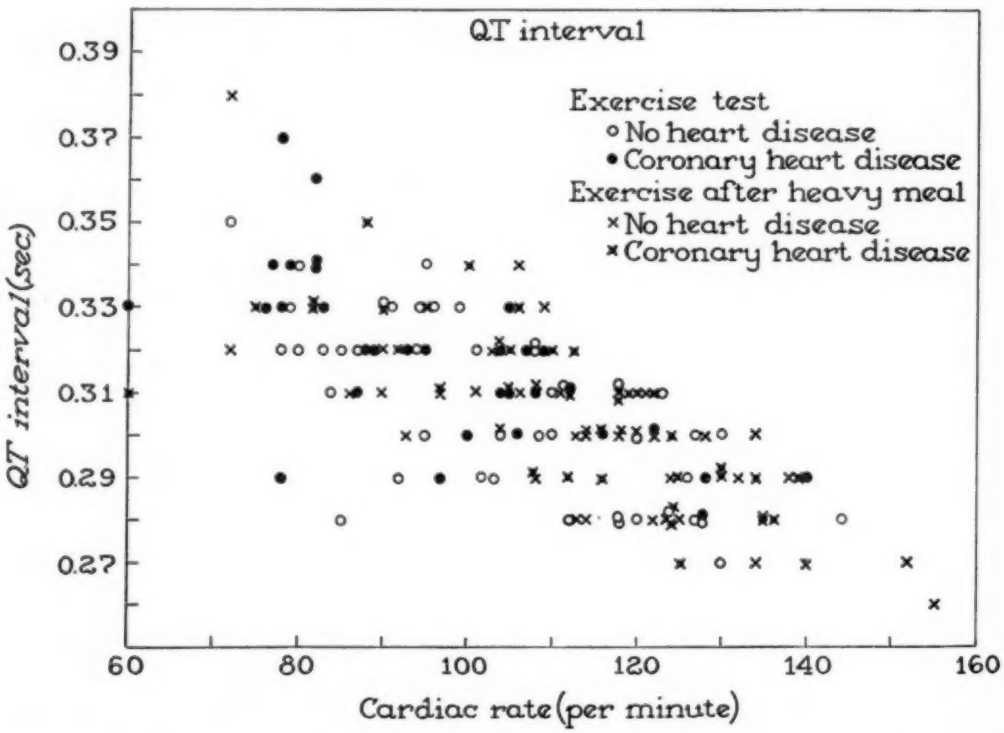


Fig. 3.—The Q-T interval is plotted against the cardiac rate. This is compared in the exercise test and the exercise test after the ingestion of a heavy meal in subjects with no heart disease and those with a clinical diagnosis of coronary heart disease.

The height of the T waves in Lead V_5 of all electrocardiograms recorded just before and just after exercise was measured. For the "resting, control" tracings in routine tests on subjects classed as having coronary disease, the mean of all T-wave heights was 2.08 mm. In the records made just after exercise, the mean of the T-wave heights was 1.85 mm. When the test was done in this same group after a heavy meal, the figures obtained for records made before and after exercise were 1.12 mm. and 1.45 mm., respectively. Similar calculations were carried out for that group of subjects regarded finally as free of

evidence of heart disease. In the routine tests, the mean T-wave height prior to exercise was 2.12 mm. and following exercise it was 2.35 mm. In tests done after a heavy meal, these values were 1.54 mm. and 1.75 mm.

These data reveal that only in the group of subjects believed to have heart disease and in tests done in the routine manner did the mean height of the T waves decrease in the records made immediately after exercise as compared with their height in tracings made prior to exercise. On the other hand, in all groups the height of the T waves was less in electrocardiograms made after the subject ingested a meal than in records made under comparable circumstances otherwise but with the subject in a fasting state.

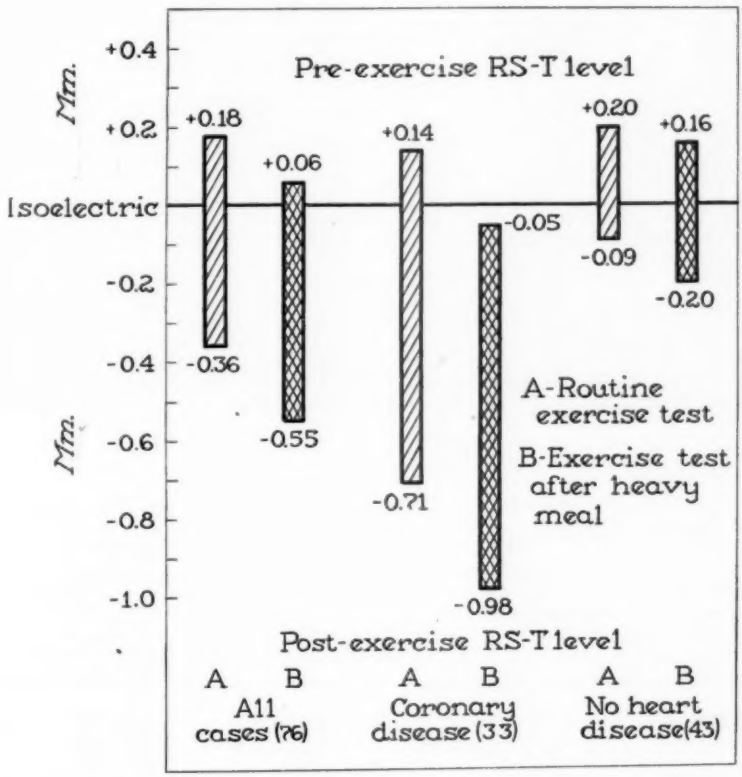
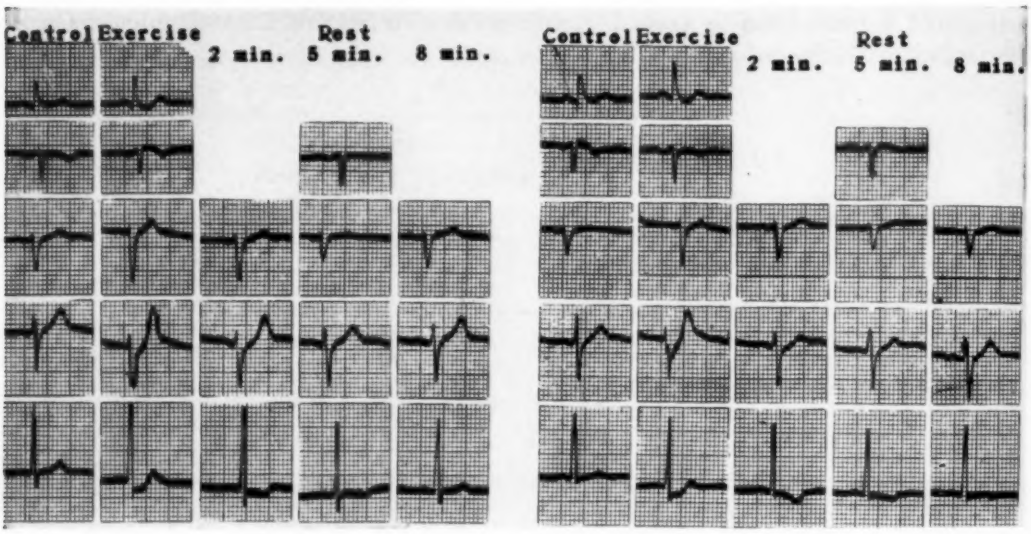


Fig. 4.—Changes in the RS-T segment in the pre-exercise and postexercise electrocardiograms. The means of the levels of the RS-T segments before and after exercise for the total group, for those with a diagnosis of coronary heart disease, and for those with no heart disease are compared in the routine exercise test and the exercise test after the ingestion of a heavy meal.

An instance in which the exercise test gave a positive result both when performed under routine circumstances and when carried out after a heavy meal is illustrated in Fig. 5. Noteworthy is the observation that the degree of inversion of TV_5 is greater and persists longer in the test done after the heavy meal. The degree of depression of the RS-T segment is not appreciably different in the electrocardiograms made immediately after exercise in the two tests.

Premature ventricular contractions were recorded in a total of fifteen subjects from the group of seventy-six. Of these, eight had ventricular premature contractions in both the tracing made when the subject was at rest before exercising and in the electrocardiograms made after exercise. Six of these eight subjects were in the group classified as being without demonstrable heart disease, and



A. *B.*

Fig. 5.—The electrocardiograms taken March 27, 1953, in the exercise test (*A*) and in the exercise test after the ingestion of a heavy meal (*B*) are shown with one complex from electrocardiographic Leads II, aV_R, V_1, V_3, and V_5. The control tracing, tracing immediately after exercise, and tracing after 2, 5, and 8 minutes of rest (A.M.) may be compared. There is a difference in the T-wave amplitude in the two tests with lower amplitude in the tracings in the exercise test (P.M.) after a heavy meal (*B*). In the latter test there is also slightly greater depression of the RS-T segment in Lead V_3. Two minutes after exercise the T wave is definitely inverted (Lead V_5) and has not returned to the pre-exercise (control) level at the end of 8 minutes. The subject made twenty complete trips over the two-step apparatus for each exercise test and complained of epigastric distress lasting about 2 minutes after each test.

two were in the group diagnosed as having coronary disease. There were six subjects who had premature ventricular beats only after exercise. There were three subjects in this group of six who were believed to have coronary disease, and three who were thought not to have that disease. One subject of the fifteen had evidence of ventricular extrasystoles only in the pre-exercise electrocardiogram. The meal alone had no predictable influence on the occurrence of extrasystoles; in fact in six instances extrasystoles were absent in the tracings following a meal when they had been present in the records of the routine test. In three patients, ventricular extrasystoles were present after the heavy meal when they were absent during the routine test.

COMMENT

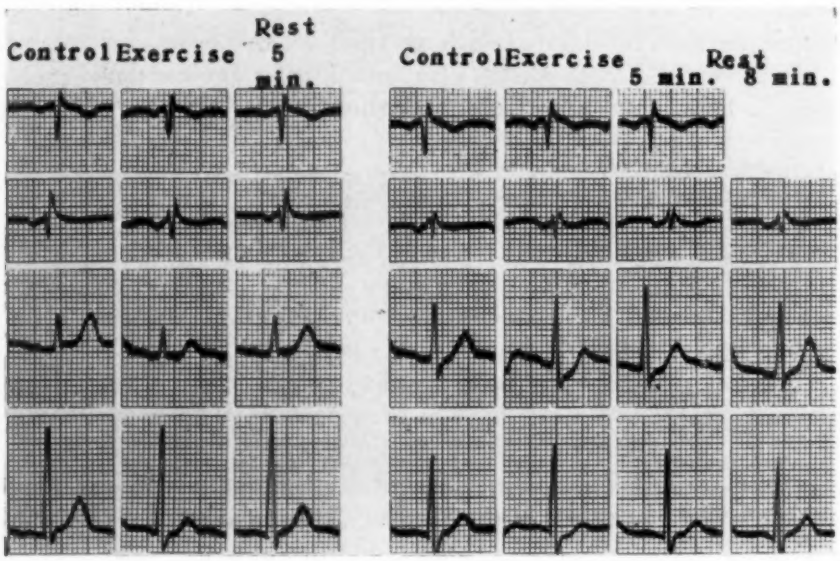
Angina pectoris is a syndrome which is commonly precipitated by exertion, emotion, or eating a large meal. In some patients the symptoms are atypical and the problem of distinguishing anginal pain from other types of chest pain may occasionally be difficult. In Heberden's original account of angina pectoris[1] the fact was noted that anginal pain came about more easily after ingestion of a meal. Wayne and Graybiel[2] in 1933-34 observed that the ingestion of food by persons suffering from angina of effort definitely reduced their tolerance for exercise, and in most it was reduced by one-fourth. When the stomachs of these same people were inflated with air their tolerance for exercise was unaffected. Riseman and co-workers[3] also noted that angina developed more readily after a heavy meal. No electrocardiographic evidence was presented by these earlier investigators.

Wilson and Finch[4] in 1923 described the effect of drinking iced water, which produced transient T-wave changes in the electrocardiogram. Gardberg and Olsen[5] reported their study of the effects of the ingestion of food on the electrocardiograms of young adults; they observed a 30 to 50 per cent decrease in the height of the T waves. The changes were maximal one hour after meals, persisted for two hours, and then began to disappear. Simonson and associates[6] in 1946 studied the effects of meals on the electrocardiogram in normal subjects. Standard mixed meals and meals high in their content of fat were attended by the same results. The consistent electrocardiographic changes were an increased heart rate, decrease in amplitude of T waves, increase in Q-T index, increase in QRS amplitude, and a left shift of the T axis. Thus food intake was considered by these authors as a major factor in the standardization of electrocardiographic procedures. At a later date Simonson and co-workers[7] described the effect of meals on the electrocardiograms of cardiac patients. In ten patients with anginal symptoms and a normal electrocardiogram before meals, the electrocardiogram became abnormal in all after the meal. The abnormality was inversion of the T wave in CF_2 or CF_4 or an increase in the Q wave in Lead II. There was no discomfort after the meal. In five patients with angina and an abnormal electrocardiogram before a meal, the electrocardiogram became more abnormal. In two patients the meal induced pain, and pronounced depression of the RS-T segment was noted especially in Lead II.

Berman[8] in 1948 observed electrocardiographic changes following meals in patients with angina pectoris. Twenty-five per cent developed 0.5 to 0.75 mm. depression of the RS-T segment and an increased concavity of this segment. Berman and co-workers[9] in 1950 reported a larger series of patients on whom results were obtained similar to those which they had reported in 1948. No member of a control group showed a shift in RS-T segment under similar conditions of study. In 20 per cent of the patients with angina pectoris, inversion of T waves in one or more leads developed during the period immediately after the ingestion of a meal. Simonson and Keys[10] in 1950 used a meal of 1,260 calories as a means of inducing "stress" in a test of cardiac function. The changes

encountered consistently were an increased heart rate, increased amplitude of R waves, decreased amplitude of T waves, and a right shift of the QRS axis.

Simonson and McKinlay[11] reported their observations of the electrocardiographic changes which attended the ingestion of meals of varying sizes by persons with and without disease of the coronary arteries. They concluded that the stress produced by a meal of moderate size is of a mild order and duplicates a situation experienced by the average person in the course of his everyday life.



A. *B.*

Fig. 6.—The electrocardiograms taken April 9, 1953 in the exercise test (*A*) and in the exercise test after the ingestion of a heavy meal (*B*) are shown with one complex from electrocardiographic Leads aV_R, V_1, V_3, and V_5. The control tracing, tracing immediately after exercise, and tracing after 5 minutes of rest (in A.M.) may be compared. The exercise-test tracings would be considered to represent a "negative" result with no depression of the RS-T segment below the isoelectric line after exercise. The tracings in the exercise test after a heavy meal (in P.M.) reveal depression of the RS-T segment in Leads V_3 and V_5, and the changes are consistent with a "positive" result. The right bundle-branch block remains unchanged. The subject walked twenty complete trips over the two-step apparatus for each test and did not develop anginal pain.

Within fairly wide limits, the electrocardiographic effects do not depend upon the composition of the meal eaten nor upon its caloric content. Changes in the tracings showed no variance in the period 20 to 60 minutes after the meal. The incidence of electrocardiographic changes deemed abnormal by the authors increased in direct relationship to supporting clinical evidence of coronary disease in the same patient. Simonson and McKinlay proposed that useful clinical information might be derived from a procedure of the type under study but advised that caution be exercised in the interpretation of results.

To our knowledge the changes in the electrocardiogram which develop in relation to exercise following ingestion of a heavy meal by the subject of the

test have not been fully investigated. Our results confirm observations reported by earlier investigators that the effects of a heavy meal alone on the electrocardiogram are particularly evident in lowered height of the T waves and increased cardiac rate. When the effects of ingesting a large meal and carrying out rather vigorous exercise were combined, the significant electrocardiographic changes most frequently encountered in the present study were depression of the RS-T segment or inversion of T waves in Leads V_3 and V_5, or both, associated with elevation of RS-T segments in Lead aV_R. Slight depression of RS-T segments in Leads aV_L and aV_F commonly appeared in association with the more striking changes in these segments in precordial Leads V_3 and V_5, but rarely in V_1. These changes are of the same order as those encountered in the exercise test as it is performed routinely, in the hypoxia test, and in spontaneously occurring episodes of angina pectoris.

To what degree must these changes be present in order that they may be held indicative of the presence of a clinical state of coronary insufficiency? The difficulties in arriving at an answer to this question have been considered in another publication.[12] Experience leads us to believe that the following changes afford adequate basis for interpreting the results of a test as positive.

1. Depression of 2 mm. or more in the RS-T segment of at least one of the recorded leads. A depression in excess of 1 mm. but less than 2 mm. in any one lead is considered to constitute an equivocally positive result.

2. Complete reversal in direction of the T waves in a left precordial lead.

To what extent were these criteria satisfied in this study when the exercise test was carried out after the subject ate a heavy meal as compared with its performance when he was in a fasting state? In one of the seventy-six subjects tested, a negative result in a test done routinely was followed by a positive result in a test performed after the subject ate a large meal (Fig. 6). As indicated in Fig. 4, the average change of the RS-T segment in Lead V_5 in subjects finally deemed to have coronary sclerosis was from a level of $+0.14$ mm. in the pre-exercise tracing to -0.71 mm. in the postexercise electrocardiogram in the exercise test as done in a routine fashion. The shift, therefore, was 0.85 mm. In this same group of subjects, in a test done after a heavy meal the shift was from a level of -0.05 mm. in the pre-exercise records to a level of -0.98 in the post-exercise tracings, a shift of 0.93 mm. The difference between an average shift of 0.85 mm. in the tests as performed routinely and an average shift of 0.93 mm. in the test done after a heavy meal is so small as to be negligible in the resolution of a clinical problem. Hence, the conclusion appears reasonable that as a laboratory aid in the diagnosis of coronary disease, no distinct advantage is to be had from performing an exercise test after a heavy meal. In rare instances, in which a young patient presents atypical historical evidence of angina pectoris and has a negative or equivocal result on the routine exercise test, repetition of the test after a meal might be considered. Patients having atypical distress confined in its occurrence to the immediate postprandial period might also be considered as possible candidates for an exercise test after a heavy meal.

CONCLUSIONS

1. A routine exercise test and an exercise test after the ingestion of a heavy meal were performed on seventy-six subjects. In thirty-eight of the men, the final clinical impression was that definite evidence of heart disease was absent, while in twenty-six a clinical diagnosis of coronary disease was made; the numbers of the women in the respective groups were five and seven.

2. The cardiac rate was higher after the heavy meal in all phases of the test, namely, in the resting control, immediately after exercise, and after 5 minutes of rest. The Q-T interval related to the cycle length remained within the normal range. When the seventy-six subjects were considered as a group, the average height of the T waves in Lead V_5 was less following a heavy meal than it was in records made under conditions otherwise comparable but with the subjects in a fasting state.

3. Only one subject having a "negative" result with the exercise test had, on a retest after a heavy meal, an unequivocal "positive" result.

4. As a laboratory aid in the diagnosis of coronary disease there is generally no distinct advantage of performing an exercise test after a meal. In rare instances, in which young patients give an atypical story and have a negative or equivocal result with the exercise test, repetition of the test after a meal might be considered.

5. Criteria for a "positive" result with the exercise test in our experience include gross electrocardiographic changes, specifically either shift in the RS-T segment of 2 mm. (normal standardization) from the isoelectric position, or marked reversal direction of T waves of large voltage in any lead.

SUMMARIO IN INTERLINGUA

Septanta-sex individuos esseva subjicite a exercitios routinari (1) in stato jejun e (2) post le ingestion de un repasto ric. Sub ambe conditiones electrocardiogrammas esseva facite ante e post le exercitio e le resultatos esseva comparate. Le ratas cardiac esseva plus alte post le repasto ric in omne phases del experimento. Le intervallo Q-T in relation al extension del cyclo se manteneva intra limites normal. Le altor median del unda T in le derivation V_5 esseva minus post un repasto ric que in le stato jejun.

Un sol individuo con un resultato "negative" durante le experimento in stato jejun monstrava un resultato inequivocamente "positive" durante le repetition del experimento post un repasto ric.

Del puncto de vista del diagnose clinic nulle distincte avantage—excepte in rar casos—resulta de executar le experimento a exercitio post un repasto.

Secunde nostre experientia un resultato positive obtenite sub conditiones de exercitio es characterisate per un displaciamento de 2 mm o plus del segmento RS-T o per un reversion complete del direction del unda T in le electrocardiogramma sinistro-precordial.

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STUDIES ON THE CONTINUOUS USE OF A CARBONIC ANHYDRASE INHIBITOR (DIAMOX) IN AMBULATORY PATIENTS

RASHID A. MASSUMI, M.D., AND JOHN M. EVANS, M.D.

WASHINGTON, D. C.

THE effect of sulfonamides on acid-base balance was recognized as early as 1937 when Southworth[1] described acidosis and hyperpnea occurring in patients treated with para-amino-benzene-sulfonamid. Marshall and his colleagues[2] produced acidosis in dogs by administration of intravenous sulfanilamide. Hober[3] perfused frog kidney with sulfanilamide and observed a shift in the urine reaction from acid to alkaline. He attributed this phenomenon to an increase in bicarbonate excretion brought about by inactivation of carbonic anhydrase. Subsequent work showed that the property of alkalinizing urine is found only in those sulfonamide compounds which possess an unsubstituted N_1 sulfonamide (SO_2NH_2) group. Beckman and associates[4] also studied the blood electrolyte changes during sulfanilamide therapy.

Sulfanilamide was shown to be a specific inhibitor of carbonic anhydrase by Mann and Keilin[5] in 1940. The extensive work of Pitts and Alexander[6] elucidated the mechanism of acidification of the urine and the role that the enzyme carbonic anhydrase plays in it. According to them carbonic anhydrase, through catalyzing the reaction $CO_2 + H_2O \rightleftarrows H_2CO_3$, increases the production of carbonic acid and, secondarily, the production of bicarbonate and hydrogen ions within the tubular cells. Consequently, the amount of hydrogen ion available for exchange with sodium ion from the content of the tubular lumen is increased, leading to augmented sodium reabsorption. When the enzyme is inactivated by an inhibitor, there will be less hydrogen ion available for exchange with sodium and, hence, increased sodium excretion.

Schwartz[7] conducted the first clinical trial with sulfanilamide and observed an increase in urinary excretion of sodium, potassium, and chloride, elevation of the urine pH and resultant diuresis. However, inasmuch as sulfanilamide was considered to be too toxic, Roblin and Clapp[8] developed a number of new heterocyclic unsubstituted sulfonamides with greater enzyme inhibitory potency and less toxicity. They introduced 2-acetylamino-1,3,4,-thiadiazole-5-sulfonamide, currently known as Diamox, as the best preparation for clinical use.

From the Department of Medicine, The George Washington University School of Medicine, Washington, D. C.

Received for publication Sept. 17, 1954.

Berliner and associates[9] administered this drug to dogs and found significant increases in urinary excretion of sodium, potassium, and bicarbonate. Friedberg and associates[10] found it useful in correcting the edema of congestive heart failure. Subsequent reports by Belsky[11] and Friedberg and associates[12] attested further to its usefulness in congestive heart failure.

Diamox has been used for relatively short periods of time in most of the published studies. The following report illustrates the results of long-term therapy in ambulatory patients with fluid retention due to congestive heart failure and other conditions.

MATERIAL AND METHOD

Thirty ambulatory patients with edema secondary to congestive heart failure (27), nephrotic syndrome (2), and venous insufficiency (1) were given Diamox* for periods ranging from 1¼ to 8½ months, with the exception of two subjects to whom the drug was administered for only 4 to 7 days. The average duration of therapy was 4 months. There were twelve males and eighteen females with ages ranging from 19 to 79 years. The average age was 58.7 years. The diagnoses represented in the group (Tables I and II) included hypertensive heart disease in eleven, arteriosclerotic in ten, syphilitic heart disease in three, thyrotoxic heart disease in one, congenital heart disease in one, rheumatic heart disease in one, nephrosis in two, and femoral venous insufficiency in one.

Of the patients with heart failure, all twenty-seven had been maintained on digitalis, mercurial diuretics, ammonium chloride, and low-salt diet for periods usually greater than one year. Diuretics and ammonium chloride were withdrawn at least four to five days prior to the initiation of Diamox. However, no changes were made in the dose of digitalis, in diet, or in any other feature of their regimen.

The patients were seen weekly or bi-weekly at which time the following determinations were made: weight, degree of edema, condition of the lung bases, subjective symptoms of heart failure, urinalysis, and blood urea nitrogen. Serum electrolyte values were determined serially before and at the completion of the three-to-five day courses of Diamox, one to six times per subject. Inquiry was made concerning the occurrence of side effects at each visit.

The daily requirement was determined according to the patient's response to an initial 250 to 750 mg. given orally in one dose in the morning for periods of three to five days weekly. In more than one-half of the subjects Diamox was given daily for ten days or more in order to compare the results of continuous regimen with those during interrupted courses of three to five days. Diamox was used as the sole diuretic as long as edema and symptoms were controlled.

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*Supplied by the Lederle Laboratories Division, American Cyanamid Company, New York, N. Y.

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RESULTS

Nineteen of the thirty patients (63.3 per cent) are still maintained on Diamox (Table I) with satisfactory control of edema and symptoms for periods ranging from 1¼ to 8½ months. Patient G. R. with leg edema due to venous insufficiency lost a large proportion of the edema with marked improvement in the varicose ulcers which had been present for many years and had failed to respond to conventional treatment. Of the two nephrotic patients, one responded well while the other remained refractory. Of the twenty-seven cardiac patients, eighteen are still taking 500 to 750 mg. of the drug daily in interrupted three-to-five day courses each week.

TABLE I. CLINICAL AND THERAPEUTIC DATA PERTAINING TO 19 SUBJECTS CONTINUED ON DIAMOX

PATIENT	AGE	SEX	DIAGNOSIS	DURATION OF TREATMENT (WEEKS)	RESULTS	SIDE EFFECTS
H. W.	66	M	H.C.V.D.	22	Good	- - - - -
T.J.	38	M	L.H.D.	26	Excellent; striking weight loss	- - - - -
W.P.	33	M	H.C.V.D.	8	Good	- - - - -
B.F.	52	F	H.C.V.D.	15	Good	- - - - -
H.W.	63	F	H.C.V.D.	8	Good	- - - - -
L.D.	65	F	A.S.H.D.	16	Good	- - - - -
W.C.	59	M	A.S.H.D.	29	Excellent	- - - - -
J.G.	61	M	H.C.V.D.	12	Excellent	- - - - -
G.V.	70	F	A.S.H.D.	12	Good	- - - - -
E.P.	66	F	A.S.H.D.	26	Good	- - - - -
C.R.	68	M	Varicose ulcers	16	Excellent	- - - - -
N.F.	71	M	L.H.D.	9	Excellent	- - - - -
E.C.	79	M	A.S.H.D.	6	Good	- - - - -
B.S.	56	F	R.H.D.	24	Excellent	- - - - -
L.C.	64	F	H.C.V.D.	23	Excellent	- - - - -
M.F.	63	F	H.C.V.D.	30	Good	Nausea and anorexia
E.H.	70	F	H.C.V.D.	22	Excellent	Transient dizziness
M.E.	19	F	Nephrosis	23	Good	Transient paresthesias
R.A.	70	M	H.A.S.H.D.	25	Excellent	Transient anorexia

Key: H.C.V.D. = Hypertensive cardiovascular disease
A.S.H.D. = Arteriosclerotic heart disease
R.H.D. = Rheumatic heart disease
H.A.S.H.D. = Hypertensive and arteriosclerotic heart disease
L.H.D. = Luetic heart disease

The amount of diuresis was striking in certain of the severely edematous subjects. However, it gradually declined as the edema subsided regardless of whether or not dry weight had been achieved. The drug has been well tolerated in this group and has created no untoward side effects. The cardiac subjects have maintained fairly constant weight. Fluctuations in weight were less marked in comparison to those encountered in the same subjects while on the conventional treatment for congestive heart failure.

The drug was discontinued in eleven of the thirty subjects (36.6 per cent) (Table II) because of severe nausea and vomiting in two, and lack of response in nine. Of the nine subjects who failed to respond, five had long-standing and recurrent congestive heart failure associated with fixed hepatomegaly and ascites. All five of these subjects had exhibited poor response to other diuretics while on ambulatory status.

TABLE II. CLINICAL AND THERAPEUTIC DATA PERTAINING TO THE 11 SUBJECTS FROM WHOM DIAMOX WAS WITHDRAWN

PATIENT	AGE	SEX	DIAGNOSIS	DURATION OF TREATMENT (WEEKS)	REASON FOR WITHDRAWAL	COMMENTS
D.K.	47	F	A.S.H.D.	31	Poor response	- - -
J.G.	63	M	A.S.H.D. Emphysema	27	Became refractory	Combination of Diamox and oral mercurial ineffectual
C.B.	64	M	L.H.D.	1	No response	- - -
M.Z.	52	F	H.C.V.D.	5	No response; abdominal pain	Combination of Diamox and mercurial injections ineffectual
A.B.	39	F	Nephrosis	2	No response	Burning and tingling in the extremities
F.S.	53	F	H.C.V.D. L.H.D.	8	No response	Poor response to all other diuretics
A.A.	69	M	A.S.H.D.	8½	Became refractory	Initial response was excellent, 14 lb. lost in 12 days
P.N.	65	M	A.S.H.D.	5	No response	Poor response to all diuretics
T.S.	44	F	H.A.S.H.D.	2	Nausea	- - -
R.M.	65	F	H.C.V.D.	4 days	Nausea and vomiting	- - -
A.S.	51	F	R.H.D.	13	No response	Poor response to other diuretics

Key: H.C.V.D. = Hypertensive cardiovascular disease
A.S.H.D. = Arteriosclerotic heart disease
R.H.D. = Rheumatic heart disease
H.A.S.H.D. = Hypertensive and arteriosclerotic heart disease
L.H.D. = Luetic heart disease

The most consistent alteration found in serum electrolytes was a fall in carbon dioxide combining power (Fig. 1). The maximum fall, 5 meq. per liter in these subjects, usually occurred after five days of continuous therapy. This, however, was not accompanied by evidence of decompensated acidosis. The changes in serum sodium, potassium, and chloride were variable and insignificant,

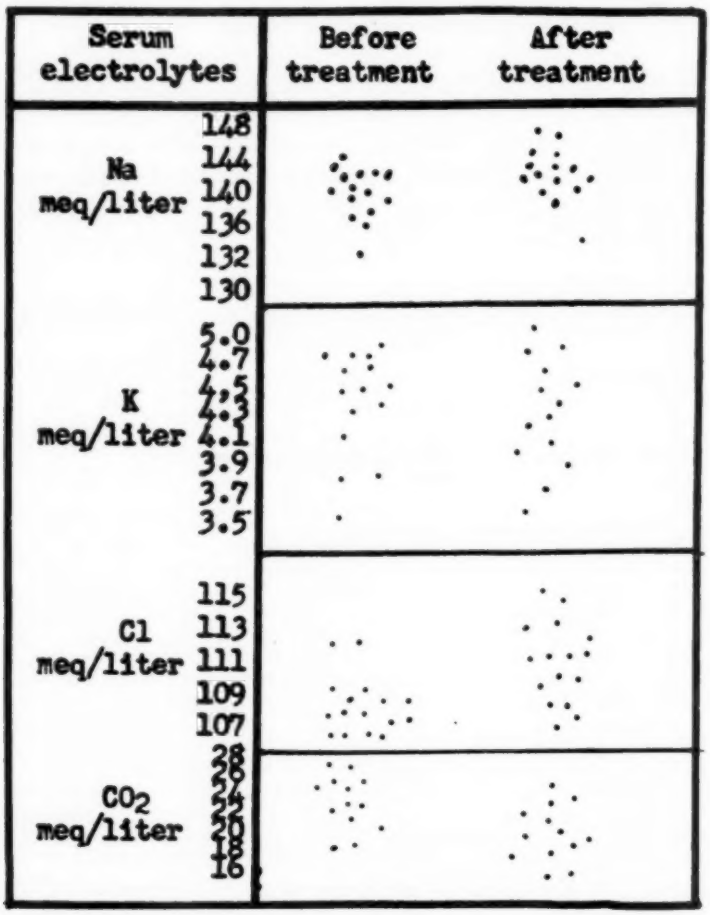

Fig. 1.—Serum electrolyte values before and after five days of therapy with Diamox.

although in occasional instances increases of chloride up to 6 meq. per liter were observed. The average rise in serum chloride was 1.7 meq. per liter. Serum sodium values did not appreciably change, and serum potassium likewise was little affected. There were no abnormal alterations of blood urea nitrogen, blood count, or urinary sediment.

SIDE EFFECTS

Side effects which appeared in nine subjects included nausea or vomiting, or both, in five, tingling and numbness in four, anorexia in three, dizziness in two, fatigue in two, and headache in one. The nausea and vomiting were suf-

ficiently severe to necessitate withdrawal of the drug in two subjects. All other symptoms were tolerable and, furthermore, gradually subsided with the continuation of therapy.

DISCUSSION

Diamox is a potent inhibitor of the enzyme carbonic anhydrase which is present in large quantities in erythrocytes, gastric mucosa, renal cortex, and in lesser concentrations in other body tissues. However, its enzymatic action apparently is not totally abolished by Diamox, presumably due to the abundance of the enzyme. In so far as the renal tubules are concerned, it is impossible to inhibit all of their acid production, as the uncatalyzed reaction continues to take place.[6] The inactivation of carbonic anhydrase in the stomach does not seem to be of untoward clinical significance. The anorexia which occurred in two subjects may have resulted from decreased acid secretion in the stomach, although it subsided in spite of continued treatment.

The diuretic potency of Diamox was striking in some subjects; one patient lost 17 pounds in three days on one occasion, and 26 pounds in seven days on another. Weight loss of 5 to 7 pounds in three to five days was not uncommon, especially in subjects with two- to three-plus ankle edema. Belsky[11] stated that Diamox had little effect in the presence of anasarca. This was not invariably true in our series, however. A more abundant diuresis was observed in patients with anasarca of recent origin, while chronic anasarca due to long-standing congestive failure associated with fixed hepatomegaly and ascites was generally refractory.

We have had no experience in treating the edema of acute or chronic glomerulonephritis. The moderate renal insufficiency commonly found in long-standing hypertensive and arteriosclerotic heart disease did not seem to influence the response.

The side effects encountered are worthy of comment. Paresthesias, dizziness, headache, nausea, and vomiting occurred one-half to one hour after ingestion of the drug at which time serum electrolyte determinations failed to show significant changes. It is suggested that a direct action on the nerve cell is responsible for these reactions. Fatigue and drowsiness, on the other hand, occurred late, were often accompanied by measurable fall in serum carbon dioxide combining power and potassium, and hence may be due to shifts in sodium-potassium equilbrium. No side effects attributable to inhibition of carbonic anhydrase in other organs were detected.

In instances when Diamox failed to effect adequate loss of edema another diuretic such as an injectable or oral mecurial was given. It was noted that such premedication with Diamox had no potentiating effect on the diuretic action of mercury. Moreover, the combination of Diamox with an oral mercurial appeared to offer no advantage over either drug given alone.

SUMMARY

1. Diamox was administered orally to thirty ambulatory patients with edema for periods of 1¼ to 8½ months. The results were good to excellent with

maintenance of satisfactory cardiac compensation in nineteen, (63.6 per cent) of the thirty subjects.

2. The response was usually less satisfactory in patients with long-standing and recurrent right-sided heart failure and fixed hepatomegaly.

3. Side effects occurred in nine subjects and were severe enough to require discontinuance of the drug in two of the nine.

4. It is felt that Diamox is a safe and effective oral diuretic for use in ambulatory patients.

5. The drug may be useful in combating edema of the nephrotic syndrome and may have a place in managing edema due to venous insufficiency.

SUMMARIO IN INTERLINGUA

1. Trenta patientes ambulatori con edema recipeva doses oral de Diamox durante periodos de inter 1¼ e 8½ menses. Le resultatos variava inter bon e excellente. Un satisfacente compensation cardiac esseva mantenite in 19 casos.

2. Le reaction esseva generalmente minus satisfacente in patientes con recurrente insufficientia dextero-cardiac de longe durantia e con hepatomegalia fixate.

3. Effectos accessori occurreva in 9 subjectos. In duo casos illos esseva satis sever pro requirer le discontinuation del medication.

4. Nos conclude que le uso de Diamox como diuretico oral in patientes ambulatori es efficace e disproviste de risco.

5. Le droga pote esser de valor in combatter edema del syndrome nephrotic e pote haber un function in le tractamento de edema debite a insufficientia venose.

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Clinical Reports

TRAUMATIC ARMOUR HEART

ERIK WARBURG, M.D.

COPENHAGEN, DENMARK

IN 1933, I published a case of traumatic armour heart.[1] Among the 261 cases of chronic pericardial lesions due to nonpenetrating traumatic injury that I had collected up to 1940,[2,3] this has been the only one of its kind, nor have I later found any similar case reported in the literature. Now, however, I have met with an additional case, and I find it reasonable to publish it as presumably such changes cannot be of altogether rare occurrence.

This patient is a luggage van guard, aged 42, who stayed in this clinic from April 17 to May 16, 1952, and from June 8 to June 16, 1953. On November 2, 1951, he had been injured in a railway accident at Brørup, where two trains running at a speed of about 60 kilometers had a head-on collision. He was in the first van, immediately behind the tender, and he was hurled up against the roof and lost consciousness.

He returned to consciousness 15 minutes later and succeeded in crawling out from under the van. He had suffered various burns from the locomotive, a long sagittal tear in the scalp, fracture of the jaw, and many smaller traumatic injuries. After this he was hoarse for a considerable length of time and had difficulty in taking a deep breath but no particular pain in breathing. His lower extremities were said to have been swollen during a period after the accident, with the edema extending up on the thighs, and he probably had a hemorrhagic exudate in the pericardium. On March 6, 1952, he was admitted to the Fredericia Hospital, from which he was transferred to the Vejle County and City Hospital, from which he was discharged on March 25, 1952. Then Dr. Kai Larsen had him admitted to our Clinic.

Physical examination showed a male, slightly overweight. Weight, 77 kilograms; 173 cm. tall. Later the weight increased to 82 kilograms. He was not cyanotic or dyspneic at rest. Moderate venous stasis in the neck. Venous pressure 150 mm. water at the first admission as well as on readmission. The liver was not palpable.

The phonocardiogram was normal.

Auscultation of the heart revealed no murmur or pericardial friction. P_2 louder than A_2. Heart action regular. No change in the position of the heart on change in posture.

Electrocardiography on admission (Fig. 1) showed slightly inverted T_I and markedly inverted T_{II-III}; axis normal and inverted T in V_{5-6}.

From the University Clinic B of Internal Medicine, Rigshospitalet, Copenhagen, Denmark. Head: Professor Erick Warburg, M.D.

Received for publication June 29, 1954.

*Read before the Danish Society of Internal Medicine on Oct. 30, 1953.

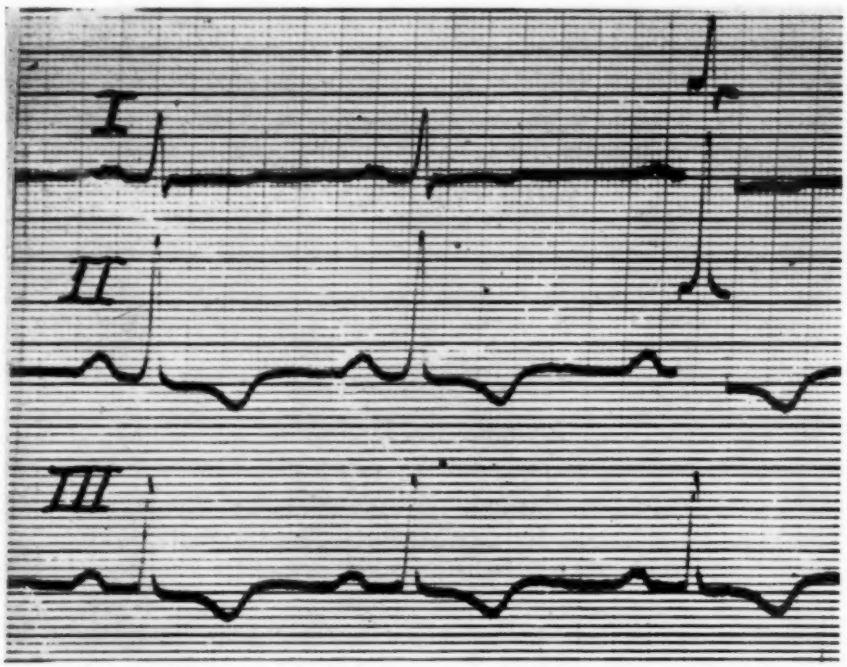

Fig. 1.—4/17/52. Extremital leads: slightly inverted T_I, markedly inverted T_{II-III}, normal axis.

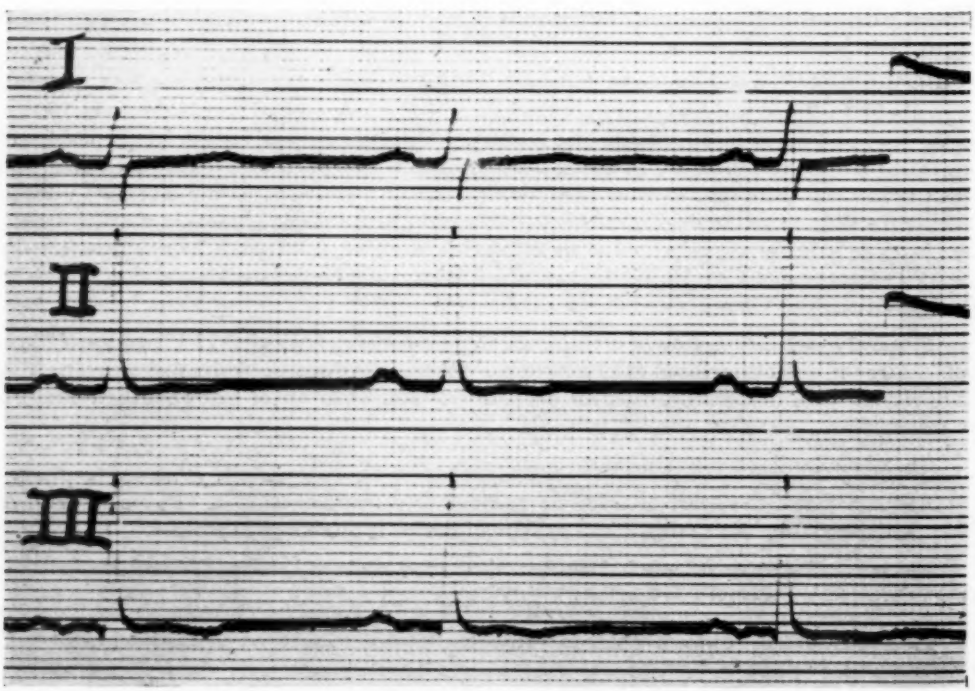

Fig. 2.—6/9/53. Extremital leads: diphasic T_I, slightly inverted T_{II}, normal axis.

On readmission (Fig. 2), the electrocardiogram showed merely diphasic T_{II} and slightly inverted T_{III}. A working ECG was performed with a load of 600 to 800 kg./min., each for three minutes, and showed no change.

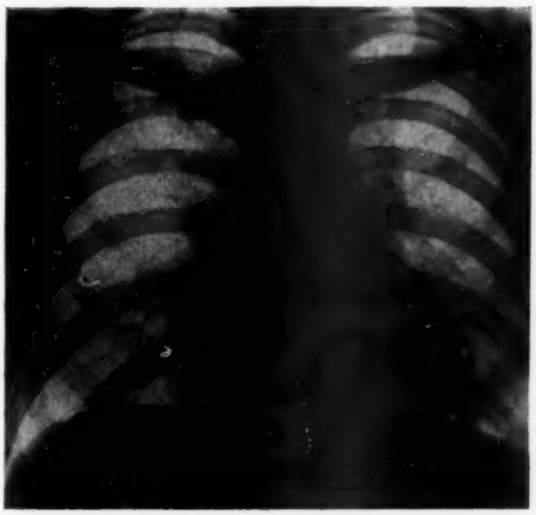

Fig. 3.—6/10/53. Heart slightly enlarged to the left.

Fig. 4.

Fig. 5.

Fig. 4.—4/19/52. Left anterior oblique diameter: pronounced calcification corresponding to the right atrium.

Fig. 5.—4/19/52. Right anterior oblique diameter: calcification upward to the right and along the diaphragmatic part of the pericardium.

Roentgenography (Figs. 3, 4, 5) showed on both admissions a slight increase in the width of the heart; in particular, the left ventricle appeared slightly enlarged. Extensive areas of calcification in the pericardium were seen. Roentgenokymography showed probably a slight reduction in the movements due to the calcification. No sign of any fracture of ribs.

Heart catheterization showed a similar change in the pressure curve for the right ventricle as described by Hansen and associates[4] in cases of constrictio cordis (Fig. 6).

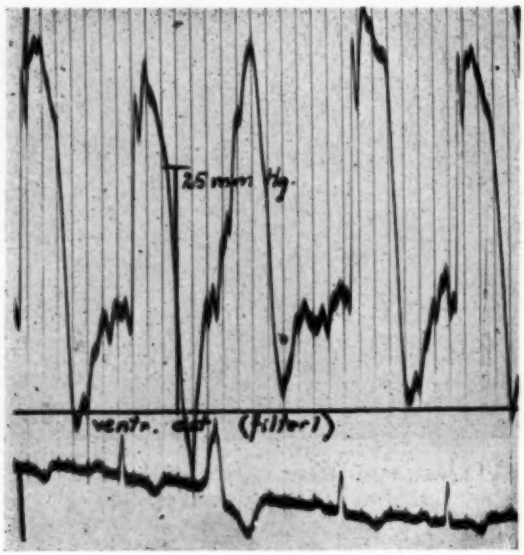

Fig. 6.—4/17/52. Pressure curve for the right ventricle. The diastolic dip of the curve is seen distinctly.

As the patient was able to attend to his usual work, no operative treatment seemed indicated.

It is of particular interest to point out the fact that the ECG changed from definitely pathologic to almost normal and that a working ECG showed no additional abnormality. This patient actually improved during observation.

SUMMARIO IN INTERLINGUA

Es presentate le caso de un homine de 42 annos de etate in qui depositos calcari, disveloppate in le pericardio post un sever trauma, resultava in le curso de un anno in un syndrome constrictive. In 1933 le autor describeva un simile caso. Ben que ille ha trovate nulle exemplos additional in le litteratura, ille crede que le condition hic describite non pote esser excessivemente rar.

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PULMONIC VALVULAR REGURGITATION

Report Of A Case With Catheterization Data

F. W. Kohout, M.D.* and L. N. Katz, M.D.

Chicago, Ill.

DESPITE the considerable interest shown in the several types of congenital and acquired heart disease since the advent and widespread use of cardiac catheterization, a dynamically significant pulmonic insufficiency is still a rare finding. In the past year, we have had occasion to make this diagnosis with certainty in one instance, and we feel that this rarity merits a presentation. An abstract of the case follows.

CASE REPORT

L. N., a 24-year-old Negro woman, was not able to furnish a reliable history. It appeared, however, that a "murmur" had been present from birth. As a child she tired easily on exertion and would then have to lie down or squat to recover. She had an almost normal life, however, and at the age of 17 became pregnant. She did well during pregnancy and gave birth to a child without difficulty. On the fourth post-partum day she had a severe uterine hemorrhage and had to be hospitalized. She was given blood transfusions and on the tenth post-partum day apparently went into heart failure which was predominantly right-sided ("swollen legs and liver"). She was given digitalis and put on a salt-free diet and recovered uneventfully, but because of this episode had her Fallopian tubes ligated. She had had two other hospitalizations, both for heart failure and for a time was taking digitalis. She voluntarily stopped taking it for the past two months and had been able to work without difficulty as a cashier in a restaurant. She still tired easily on exertion. She was seen in the hospital for some unrelated complaint and the diagnosis of heart disease was made, for which reason she was referred to the Heart Station for further study.

The patient was normally developed and somewhat overweight. There was no dyspnea, cyanosis, or clubbing. The chest was normal. Pulse was 86, and blood pressure was 100/70 mm. Hg. The apex beat was displaced to the left but not downward. There was a systolic thrill, best felt at the pulmonic area, but also present along the left sternal border and to the left, almost to the apex. A loud rasping, Grade 4 holosystolic murmur could be heard over the anterior aspect of the chest, best at the pulmonic area. The second pulmonic sound was absent. The second aortic sound was normal. A short, rough, early diastolic murmur, about Grade 3, could be heard around Erb's point. No other murmurs were present. The peripheral pulses were small but definitely present. No signs of aortic insufficiency were found.

The electrocardiogram, Fig. 1, showed a sinus rhythm, normal P waves, marked right-heart strain and right-sided conduction defect. The phonocardiogram showed the two murmurs

From the Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago, Ill.

Aided by the Michael Reese Research Foundation and the National Heart Institute (H-218).
Received for publication Oct. 12, 1954.

*Formerly Senior Resident in the department.

described; the systolic murmur occupied all of systole and was high-pitched, while the diastolic murmur was short, occupied the early part of diastole, and was lower pitched.

Roentgenograms and fluoroscopy showed that the heart was enlarged mainly to the left, and that the apex appeared to be lifted off the diaphragm. The pulmonary artery segment was quite prominent and pulsated vigorously. The hilar shadows were increased, and a hilar dance was definitely present. The rest of the lung fields did not appear to be hypervascular. Enlargement appeared to be predominantly right ventricular. The aorta was normal in size and did not pulsate vigorously. The left auricle and the diaphragm appeared to be normal.

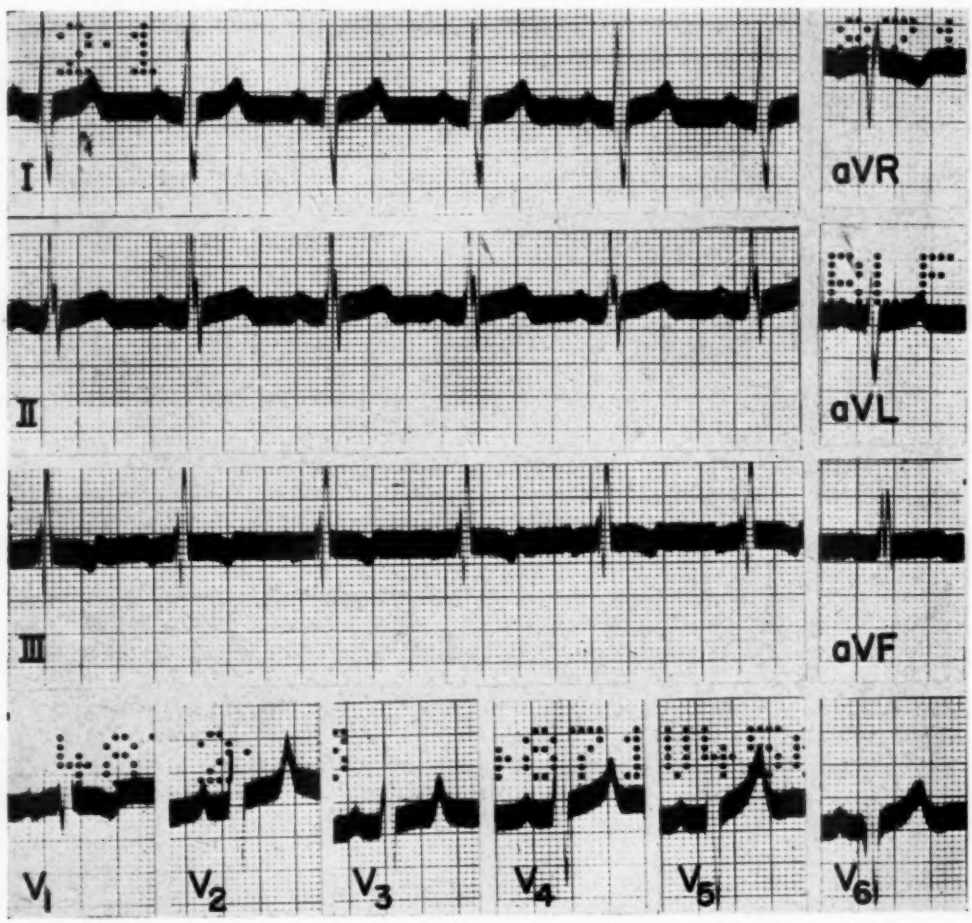

Fig. 1.—Electrocardiogram showing right-heart strain and a right-sided conduction defect.

The precatheterization diagnosis was trilogy of Fallot.

Cardiac catheterization was performed on Nov. 10, 1953. The catheter was inserted through a left antecubital vein and could be passed as far as the pulmonary artery. The catheter did not take any abnormal pathways. The findings are summarized in Table I. Oxygen consumption was not determined because the patient was emotionally upset and could not tolerate the mask.

As can be seen from Table I, there is an increase in the oxygen content of the right ventricular and pulmonary arterial samples, as compared to the caval and right atrial samples. This most strongly suggests the presence of an interventricular septal defect with a left-to-right shunt. The normal saturation of the systemic arterial sample rules out the existence of any significant right-to-left shunt.

TABLE I. CATHETERIZATION DATA

LOCATION		OXYGEN CONTENT (VOL. %)*	PRESSURES (MM. HG)†	
I. V. C.		13.4		
		13.3		
S. V. C.		13.0		
R. A.	high	12.5	8/−2	M: 2
	mid	13.5		
	mid	13.2		
	low	13.6		
R. V.	low	14.7	100/5	
	mid	16.4		
M. P. A.		—	50/5	
R. P. A.		14.1	20/5	M: 10
L. P. A.		15.4	30/5	M: 12
P. V. C.		18.4		M: 7
B. A.		18.6 (93.5% saturated)	100/70	

*Determined according to the technique of Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurements, J. Biol. Chem. **61**:523, 1924.

†Recorded with a Sanborn electromanometer.

I. V. C. is inferior vena cava; S. V. C., superior vena cava; R. A., right atrium; R. V., right ventricle; M. P. A., main pulmonary artery; R. P. A., right pulmonary artery; L. P. A., left pulmonary artery; P. V. C., pulmonary artery wedge; B. A., brachial artery; and M, mean blood pressure.

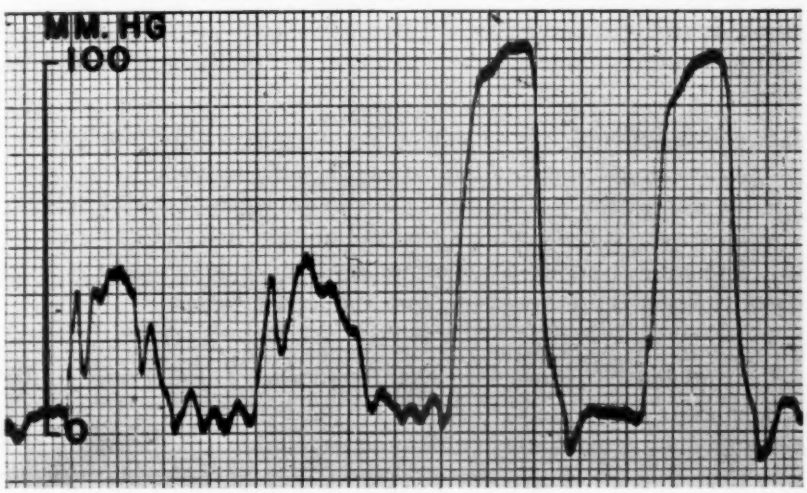

Fig. 2.—Pressure curves obtained as the catheter was withdrawn from the main pulmonary artery (the two complexes to the left) into the right ventricle (the two complexes to the right). Note the difference in the systolic levels and the similarity in the diastolic levels. Also note the steep catacrotism in the pulmonary artery curve followed by a horizontal stretch close to the level of the ventricular diastolic pressure. The pulmonary artery pressure curve is distorted by artifacts engendered by the pulmonary stenosis.

The pressures in the right atrium are within normal limits. The systolic pressure in the right ventricle is markedly elevated, and there is a distinct gradient between the systolic pressure in the right ventricle and the elevated systolic pressure in the main pulmonary artery. This can best be seen from Fig. 2, which represents a continuous pressure recording while the catheter was withdrawn from the main pulmonary artery into the right ventricle.

The curves show artifacts due, in all probability, to the considerable whipping of the catheter, which was plainly seen on the fluoroscopic screen. Despite this, the high systolic pressure level in the pulmonary artery can easily be made out. More important, in that it establishes the diagnosis of pulmonic insufficiency, is the abrupt steep slope of the catacrotism to a diastolic value practically identical with that in the right ventricle, and the remainder of the diastolic portion of the pulmonary pressure curve is horizontal. The right ventricular curves aside from their large magnitude can be considered to be of normal contour.

This pulmonary artery pulse contour was not an artifact. The maneuver was repeated several times, and the result was always the same.

DISCUSSION

True organic pulmonic insufficiency is rare. The pulmonic valve and cusps are not usually involved by acute rheumatic fever or subacute bacterial endocarditis. On the other hand, a congenital malformation almost always leads to stenosis, either valvular or infundibular. Unlike rheumatic mitral stenosis, a stenosis of the pulmonic valve ordinarily is not associated with a significant insufficiency. There have been reported cases of pulmonic valve insufficiency due to aneurysms of the pulmonary artery and distention of the pulmonic valve ring by aortic aneurysms. Among the more unusual causes of pulmonic insufficiency reported is one in which a subendocardial hemorrhage following a horse-kick to the chest lead to regurgitation with no rupture of the cusps,[1] another due to ulcerovegetative typhoid endocarditis of the pulmonic cusps,[2] and still another due to infestation of the pulmonary artery by echinococcus cysts.[3]

Relative or functional pulmonic insufficiency is said to be much more common and is usually invoked to account for an otherwise unexplainable diastolic murmur in the pulmonic area. This occurs in the presence of septal defects or other valvular lesions, particularly when large pulmonary arteries are seen roentgenologically. The dilatation of the pulmonary artery leading to stretching and deformity of the ring is presumed to cause the regurgitation.

The Graham Steell murmur[4] is the classical example of such a functional pulmonic insufficiency. However, the diagnosis of functional pulmonic insufficiency is still controversial,[5] and, as stated by Friedberg,[6] " . . . .statistics as to its occurrence are extremely varied and unreliable." Furthermore, Dressler[7] points out that " . . . .the essential sign of organic pulmonary regurgitation, that is, a collapsing pulse of the pulmonary (hilus) vessels, is usually missing in those cases."

Too many of the reports of pulmonic valve regurgitation in the past have been based in part on the necropsy finding of a dilated pulmonic valve ring or of an abnormal number of pulmonic cusps. The assumption that a dilated ring at necropsy indicates pulmonic insufficiency must be viewed with caution, since measurements at necropsy need not necessarily reflect conditions in life, as was clearly shown by Kissin's report.[8]

Prior to the widespread use of cardiac catheterization the diagnosis of pulmonic insufficiency had always been made by exclusion, because of the absence

of any objective measurements, to explain a blowing "insufficiency-like" diastolic murmur best heard along the left sternal border. The differential diagnosis involved exclusion of aortic insufficiency, and this required the absence of any signs of a dynamically significant aortic regurgitation.[9] However, an acoustically significant, but dynamically insignificant, aortic regurgitation cannot be excluded in this way with certainty.

Lately it has become important to consider the possibility of pulmonic insufficiency in the differential diagnosis between interventricular septal defect and patent ductus arteriosus, both with left-to-right shunt. The often reported contamination of right ventricular blood by systemic arterial blood from a patent ductus arteriosus confuses the catheterization diagnosis, and a functional pulmonary valve insufficiency, no longer demonstrable after surgery, is the alleged cause of this contamination. This is so particularly when, during cardiac catheterization, the catheter does not take any abnormal course that will establish the diagnosis (i.e., passage through the septal defect or through the ductus), or if dye dilution techniques are not employed. In such an event, the picture in both conditions may be quite similar, and inspection of the pulmonary arterial pressure pulse contour obtained in the pulmonary artery may be very helpful.

The necessity for an accurate diagnosis becomes apparent when one considers that surgical ligation of the patent ductus arteriosus has been an accepted procedure for some time, while surgery of interventricular septal defects is not, as yet, commonly carried out.

One instance of right ventricular and pulmonary arterial diastolic pressures being low and equal, attributed to pulmonic valve insufficiency, has been reported in a case of interventricular septal defect with pulmonary hypertension.[10] A case of Eisenmenger's complex with pulmonary regurgitation due to congenital absence of the pulmonary valve cusps had the characteristic murmur but unfortunately was not catheterized.[11]

In our own case, the low pulmonary diastolic pressure and the pulsating pulmonary artery segment in the presence of a picture otherwise typical of pulmonic stenosis might suggest the diagnosis clinically. Also when the rigid stricture of the pulmonic valve in valvular pulmonic stenosis is considered, one wonders why pulmonary valve insufficiency is not more commonly seen in mild cases.

SUMMARY

A case is reported which on catheterization gave evidence of an interventricular septal defect and a pulse contour indicative of pulmonary valve stenosis associated with a dynamically significant pulmonic insufficiency. The pulmonic valve insufficiency was identified by a characteristic pulse contour which is described. It is rare to make the diagnosis of pulmonic insufficiency with any degree of certainty during life.

SUMMARIO IN INTERLINGUA

Es reportate un caso in que le catheterisation indicava le presentia de un defecto del septo interventricular e de un configuration del pulso que permitteva le diagnose de un stenosis del valvula pulmonar associate con un dynamicamente significative insufficientia pulmonic. Le insufficientia del valvula pulmonic esseva identificate super le base de un configuration characteristic del pulso. Isto es describite. Le caso debe su interesse al raritate de casos de insufficientia pulmonic con plus o minus definitive diagnosis executate durante le vita del patiente.

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Book Reviews

HEART DISEASE AND INDUSTRY, With Particular Reference to Workmen's Compensation Case, By Meyer Texon, M.D., with forewords by Samuel A. Levine, M.D., and Hubert W. Smith, LL.B., M.D. 324 pages, New York, 1954, Grune & Stratton, Inc.

The main theme of this book is the lack of cause-and-effect relationship between physical exertion and coronary occlusion, which the author states " . . . is the expected natural result of antecedent coronary artery sclerosis." This leitmotiv is developed by means of 100 case histories which constitute over three-fourths of the bulk of this volume; they are given in great detail, and occupy an average of two and one-half closely printed pages each. At the outset, the author lists the problems involved, for instance, the importance of differential diagnosis, chronologic relationships, the effects of remote trauma, rehabilitation problems, etc., and states by which of the case histories they are best illustrated. Then, at the beginning of each history, he lists the problems which it illustrates. The third and last section discusses coronary occlusion in detail, and includes short paragraphs on numerous subjects, such as other types of heart disease (Hypertensive heart disease is dismissed in about 140 words, congestive heart failure in 37.), the rehabilitation of cardiacs, etc.

The illustrative material is well chosen, and does exemplify the varied factors which must be kept in mind when assessing a patient with coronary heart disease from the point of view of compensation and rehabilitation. One might wish that the author had spent more time on other facets of the problem; he seems to belabor mercilessly his major premise, namely that exertion in the course of employment does not bring about coronary occlusion, and devotes so little space to other subjects that the title would seem to be misleading.

The volume is meant to help physicians, lawyers, insurance companies, and compensation boards decide the compensability of coronary disease; this stated aim is accomplished successfully.

G. R. T.

MYOKARDSTOFFWECHSEL UND HERZTHERAPIE. By Dr. Fritz Pendl, 248 pages with 26 figures. Stuttgart, 1954, Georg Thieme.

This is a book written by a therapeutic enthusiast who, fascinated with the rapid advances in physiology and biochemistry during the past two decades, tries to translate them summarily into the practice of treatment of heart disease.

The author renders a very diligent though not very critical review of the newer, chiefly German, literature on muscle metabolism and the role of derangements of the electrolyte balance, the plasma protein composition, and the carbohydrate metabolism of vitamin deficiencies and hormonal imbalances. These data are followed by speculations as to the advisability of the administration of various substances (such as potassium, calcium and phosphorus, adenosinetriphosphatase and monophosphate, crude liver extracts, vitamins B_1, B_6, B_{12}, C, and E, cocarboxylase, sugars, especially levulose, cortisone in small doses, Eschatin, etc.) in cases of congestive heart failure, angina pectoris, myocardial infarction and various arrhythmias. The case reports quoted to illustrate the effectiveness of these measures are entirely unconvincing. Almost every case described suggests a different interpretation of the "success" of treatment e.g., spontaneous reversal to regular sinus rhythm (p. 186) and subsidence of digitalis toxicity (p. 221).

Many case reports are difficult to evaluate because of the loosely used terminology of heart disease (e.g. ". . . case of severe endocarditis with bundle branch block and evidence of cardiac decompensation on the basis of periapical granuloma . . . ") or because of the extensive use of proprietary names for the preparations employed. In other cases so many different drugs are used simultaneously (p. 37) that no clear-cut conclusion appears possible. In no case does the reader get the impression that optimal standard treatment had been employed.

The reviewer did not, as he had expected, receive some unorthodox but provocative ideas from reading this book, but rather an uncomfortable feeling as to the likely results of injudicious and overzealous therapeutic activity.

A. V.

ATLAS POSTMORTALER ANGIOGRAMME. By J. Schoenmackers, and H. Vieten, Stuttgart, 1954, Georg Thieme.

This book consists of the illustration and discussion of 131 angiograms selected from a total material of 1,452 x-rays of 312 cases in whom intravascular injections of various radiopaque suspensions, usually barium sulfate, were made post mortem. The appearance of arteries and veins of medium and small size in normal states and a variety of abnormal states was investigated with the organs in situ. With the technique used, vessels down to a caliber of about one millimeter are demonstrated. No comparison with clinical angiograms is attempted, and the great vessels and chambers of the heart are not discussed. The latter was deliberate because the present atlas was conceived as complementary to the atlas of Laubry and associates ("Radiologie Clinique du Coeur et des Gros Vaisseaux," Paris, 1939, Masson). Nevertheless, there is considerable information of interest to the cardiologist, some of it with physiological implications. Thirty illustrations are devoted to the arterial system of the lungs, twenty-two of the brain, twelve of the heart, ten of the kidneys, twenty-two of the trunk, and three of the fetus. The portal circulation was illustrated twenty times, and there are twelve systemic venograms. The illustrations are of excellent quality. Appended to each chapter are additional summaries in English, French, and Spanish. There is a brief bibliography and an index.

Distinctive changes throughout the circulation are demonstrated in hypertension (lengthening and tortuosity of arteries, increased caliber, and stepwise rather than a smooth decrease in size with peripheral progress). These changes are noted with pulmonary hypertension as well as with systemic. The limits of demonstrability of vessels with this technique are shifted peripherally by hypertension due to dilatation of small arteries that are not ordinarily opacified, so that more arteries appear to be present. The latter change tends to be masked by arteriosclerosis or edema. A similar peripheral shift of visibility with a false impression of an increased number of smaller arteries is seen in cyanotic congenital heart disease, although in this case the larger proximal arteries are not dilated. A similar shift toward visibility of smaller radicles without dilatation of the main trunks is seen in both the portal and caval venous circulation if cyanosis is present. These changes are seen in all organs of the body, but especially in the kidney. Severe congestive heart failure without cyanosis may also produce a peripheral shift of visibility of the caval venogram, but there is also a tendency to an absolute increase in the number of small veins, as well as varicosities of veins near the thoracic spine and various portocaval anastomoses below the level of the diaphragm. (Portocaval anastomoses both above and below the diaphragm and passing through it could be demonstrated in portal hypertension.) Collateral circulation in congenital heart disease and coronary artery disease is also well demonstrated. The authors were led by their material to the conclusion that significant rotation of the heart about its long axis was more often due to atrial enlargement than ventricular, with right atrial enlargement producing clockwise rotation and left atrial enlargement counterclockwise. The vascular effects in the various organs of tumor, infection, arteriosclerosis and many other conditions are depicted. The book can be recommended as a careful and technically expert contribution of interest to the cardiologist and many others.

G. H. W.

HEART: A PHYSIOLOGICAL AND CLINICAL STUDY OF CARDIOVASCULAR DISEASES. By Aldo A. Luisada. Ed. 2. Baltimore, 1954, The Williams & Wilkins Company.

The reviewer of the initial edition of this book (October, 1951) found that it presented implications and conclusions at some variance with classical concepts. Such differences of opinion may often be refreshing or productive. These features in the present edition may be condoned. Not so, however, the inaccurate presentation of factual data or the introduction of opinion as fact. In the chronology presented in the opening chapter, for example, the unipolar electrocardiogram is credited to Goldberger rather than to its true originator. Angina pectoris is described as a precordial pain; nothing is said about its classical location in the substernal region. A pericardial friction rub is stated to be present in acute myocardial infarction only when the infarct is anterior in location. The statement that in ventricular septal defect the area of cardiac dullness becomes nearly round betrays a naive faith in the possibilities of cardiac percussion. Unwarranted confidence is placed in the direction of transmission of murmurs in determining their significance. (The focal glomerulonephritis of Loehlein, and not the diffuse glomerulonephritis of more recent writers, is considered the most constant renal lesion of subacute bacterial endocarditis.) The discussion of the electrocardiogram in acute cor pulmonale omits mention of transient incomplete right bundle branch block or of the possibility of confusion with acute posterior myocardial infarction. In the sections on therapy, papaverine is still presented as of value in favoring the establishment of a collateral circulation; this view is no longer tenable. Inhalation of oxygen-alcohol vapor, a treatment in which the author has been interested, is presented as the therapy of choice for acute pulmonary edema; this view is not yet universally accepted. One may also disagree with the injunctions that during an acute attack, mercurials should be limited, or that digitalis should not be given by vein.

The author, for years a student of the mechanical registration of phenomena associated with the heart beat, exercised admirable restraint in the handling of this general subject. The reading of these sections will be rewarding to the interested reader. Also, this volume serves as an excellent introduction to the continental experience and point of view. The sections on tricuspid disease, for example, are particularly well done.

The uneven quality of this book raises the question whether, in view of the very high degree of specialization and subspecialization current in cardiology, the experience of any observer can encompass enough of the entire field to enable him, single-handed, to cover the subject authoritatively or even competently. One would hesitate to recommend this book unreservedly.

H. D. L.

THE YEARBOOK OF MEDICINE. 1954-55 Series. Chicago, Ill., The Yearbook Publishers.

This annual review of recent literature in the field of internal medicine is a most useful summary of some of the more significant contributions in this field. The value of such a volume is determined, among other things, by the care used in the selection of articles to be abstracted and also by the caliber of the critical comment of the editorial staff which follows many of the abstracts. It is a pleasure to say that the editorial staff have done a fine job in commenting on this series of articles. In general, with some exceptions, the selection of articles that are summarized is a representative sample of the better contributions in the literature. The section on cardiovascular disease is an excellent one. The only criticism that might be made of this section is that more articles dealing with a physiologic type of investigative work could have been incorporated. However, in a volume intended primarily for clinicians, it is inevitable that the major portion of the work considered would be of a clinical rather than a physiologic nature. This book will be of interest to cardiologists and to internists generally.

H. E. H.

LA VALVOLA MITRALE. By M. A. Chiechi and Ch. P. Bailey. Roma, 1954, Il Pensiero Scientifico, 558 pages and 158 figures. Price 5,000 lire.

This interesting Italian monograph is devoted to the study of the mitral valve. In collaboration with Dr. Bailey it has been prepared by Dr. Chiechi, a young Italian surgeon who worked in New Jersey and Pennsylvania.

The material analyzed in this book consists of 753 cases studied in detail out of a total of 1,200 cases of mitral valve disease.

The most interesting chapters are: (1) a detailed historical study; (2) a new investigation on the morphology of the mitral valve in 105 normal hearts which led the authors to the conclusion that the so-called commissures are either additional small leaflets or continuous endocardial tissue between the two main parts of the valve; (3) a clinical study of the patients to be selected, of the results of surgery, and of the diagnostic criteria.

Less well developed are: (a) the dynamic aspects of the valvular defect; (b) the diagnostic methods of recognition of mitral stenosis.

The various surgical details of the mitral valve operation, even though well described, are less well illustrated than in other publications of Bailey.

Among the interesting details discussed in this book, mention should be made of gross and microscopic studies of the "atrophic" left ventricular wall.

In conclusion, this is an interesting contribution which may be read to advantage by those cardiologists and surgeons who are familiar with the Italian language.

A. A. L.

Announcements

The AMERICAN COLLEGE OF CARDIOLOGY will hold its fourth annual convention at the Hotel Biltmore in New York City on May 18 to 20, 1955. Two scientific sessions will be devoted to a symposium on HYPERTENSION AND HYPERTENSIVE HEART DISEASE. Another scientific session will be devoted to ADVANCES IN CARDIAC SURGERY and a fourth session to the HEART AND CIRCULATION IN SPORTS. In addition to symposia and panel meetings, there will be scientific exhibits on cardiovascular research and commercial exhibits, outlining the latest advances in the field of cardiology. Dr. Ashton Graybiel, Pensacola, Florida, will preside. Any program information may be obtained from the Secretary of the College, Dr. Philip Reichert, 140 West 57 Street, New York 19, N. Y.

The 1955 meeting of the AMERICAN GOITER ASSOCIATION will be held in the Skirvin Hotel, Oklahoma City, Oklahoma, on April 28, 29, and 30, 1955.

The program will consist of papers and discussions dealing with the physiology and diseases of the thyroid gland.